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THE STORY OF THE MELBOURNE SCHOOL OF PATHOLOGY.[1]

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I shall be content if those who desire to give a view of events as they really happened shall pronounce my History useful.

—Thucydides: *Historia*, Book I, Section 2.

A DISCUSSION of pathology, the study of disease, usually conjures up in people's minds a vision of something unpleasant or even offensive. This misleading legend is one which I propose to deal with at another time; but tonight we will confine our attention to the local historical rather than the scientific aspect of the subject.

It is important that some statement of the history of our school should be made at this time. The older members of the medical profession have been passing from us, and with them a great deal of valuable and entertaining information is going and some has gone beyond recall. I myself have seen many changes in the pathology department, but necessarily have had to learn much from my seniors. However, though I have not the first-hand knowledge of a Thucydides, perhaps we are sufficiently near the beginnings for history not yet to have "faded into fable", nor for it to be merely "a distillation of rumour".

[1] An inaugural lecture, delivered at the University of Melbourne on June 25, 1951.

Henry Ford, during a court case in 1919, made his famous oft-quoted remark: "History is bunk." We know how the account of events may be distorted even by intelligent and apparently unbiased observers. This occurs because any event has numerous small components, any one of which may be given undue prominence. Recently the American commentator Raymond Gram Swing (*Saturday Review of Literature*, June 3, 1950), in an entertaining summarized estimate of history, emphasized that any simple statement must necessarily be incomplete. Any event must be considered therefore from the point of view of its many components, and each of these consists of the story of an individual. This was indicated in Emerson's statement: "There is properly no history, only biography." The same idea was put forward by Carlyle: "History is the essence of innumerable biographies."

Here we shall consider a composite picture containing portraits of many of the best-known medical graduates of the last seventy years. Some are sketched very lightly, though others stand out in bold relief, and of these the two most prominent are the two professors of pathology.

As the early development of the pathology department can be appreciated only if we understand the beginning of the University of Melbourne itself as well as of the Medical School, these will be discussed first. The district of Port Phillip was separated from New South Wales and converted into the Colony of Victoria in 1851, and in January, 1853, Mr. H. C. E. Childers, the Auditor-General, introduced a Bill to establish and endow a university. The University of Sydney had been incorporated in October, 1850. Thus the University of Melbourne was begun at a very early period in the development of the State; the foundation stone was laid on May 13, 1855.

It is important that a Dr. Anthony Colling Brownless was gazetted a member of council on June 16 of this year (1855). The chancellor, Mr. Justice Redmond Barry, was, of course, interested in the formation of a law school; but Dr. Brownless was a strong protagonist for the development of a medical school. In 1858 he became vice-chancellor.

In 1859 there were two events of importance. One was the appointment of Dr. T. S. Ralph (who was later for many years president of the Microscopical Society of Victoria) to the position of collector of anatomical, physiological, pathological and botanical specimens. The other was the formation of a Medical School Committee. This committee consisted of the vice-chancellor, Dr. Brownless, Sir Francis Murphy, who was a member of the Royal College of Surgeons and the first speaker of the Legislative Assembly, the Honourable W. C. Haines, who had practised as a surgeon in England and who was the first premier of Victoria, and Sir James Palmer, a medical man who was the first president of the Legislative Council and president of the Melbourne Hospital, amongst others. It will be appreciated that there was a large body of influential opinion to give necessary weight to the proposal for the formation of the medical school.

In 1862 the chancellor, who was visiting England, was empowered to obtain opinions from Professor Paget and Professor Owen in choosing a professor of anatomy, physiology and pathology. This matter has been discussed elsewhere, and we need not go into details; but George Britton Halford was appointed to this post. The medical school was opened on March 3, 1862, seven years after the foundation stone of the university had been laid. The medical school was the first one to be formed in Australia; the Sydney school did not begin until 1883, when a chair of anatomy and physiology was formed (Professor T. P. Anderson Stuart being appointed).

Professor Halford gave his introductory address on May 1, 1863. The original medical school buildings, completed in May, 1864, were on the site of the present physiology school. The curriculum for fourth year was general anatomy, physiology and pathology, dissections, medicine, obstetrics and diseases of women and children; but at this time there was no organized pathological teaching even in the post-mortem room. Pathology was represented only by scattered references in the courses of physiology, medicine and surgery, and this state of affairs remained until 1881. Lecturers were appointed in the various subjects.

An important appointment was that of James Edward Nield, M.D., in 1865, as lecturer in forensic medicine. Almost every subject in the medical course has been changed considerably over the years—by combination with other subjects, by alterations in its place in the course, and by changes in the status of lecturers. However, forensic medicine has escaped such vicissitudes and stands alone in showing a definite and clear-cut lineage from the beginnings of the medical school until today. The experienced student of the subject knows that truth is stranger even than detective fiction, so that, in a wicked world, the continuous presence of an efficient department of forensic medicine has been, and is, a matter of greatest import to the community.

Dr. Nield, keen-eyed, beetle-browed and somewhat bald, was a strong personality with wide interests both within and outside the profession. For many years he was librarian to the Medical Society of Victoria, and he was its president in 1868; he was editor of the *Australian Medical Journal* from 1862 to 1879. He contributed many articles on musical and dramatic criticism to the lay Press. Withal he had a very large practical forensic experience and was the chief expert assisting the city and district coroners.

In 1870 a Mr. W. Smith, M.B., was appointed demonstrator in anatomy and curator of the pathological museum at the Melbourne Hospital. It is from this museum that the museums in the present departments of anatomy and pathology at the university stem.

In 1871 Harry Brookes Allen entered the medical school—a very important event, because he was to play a leading part in the development of the school and was to initiate and then mould the department of pathology. He was born in Geelong on June 13, 1854; he was educated in Geelong and later at the Church of England Grammar School and entered our medical school at the age of eighteen years. He has told us of the primitive conditions existing at that time. There was no proper first-year science; no medical student could attend classes in natural philosophy and there were no separate teachers of biology. There were no students' laboratories in the whole university except the dissecting room. Allen graduated in 1876 (in which year the Faculty of Medicine came into being), and immediately showed his interest in the problems of teaching in this school. In May of that year he was given charge, in part, of the dissecting room; later in the year he became demonstrator in anatomy and subconservator of the university museum of anatomy and pathology, and almost at once was appointed pathologist to the Melbourne Hospital. His interest in pathology manifested itself in demonstrations of pathological material both in the dissecting room and at the hospital, and these demonstrations became widely known and long remembered.

From the beginning his interests were wide. In 1879 he was lecturer on *materia medica* and therapeutics during the temporary absence of Dr. Dougan Bird. In the same year he was honorary secretary to the Medical Society and later played an important part in the union of the Medical Society with the Victorian Branch of the British Medical Association. From 1879 to 1883 he was editor of the *Australian Medical Journal*. It may be noted that in 1879 the foundation stone of Wilson Hall was laid.

In 1880 Harry Allen undertook the lectures in anatomy and physiology while Professor Halford was in England, and on his return in 1881 Dr. Allen was appointed lecturer in anatomy and pathology. In the next year (1882)—the year in which Robert Koch discovered the tubercle bacillus—Harry Allen was appointed professor of descriptive and surgical anatomy and pathology, Professor Halford becoming professor of physiology and histology. It is probable that the division in this manner and the combination of pathology with anatomy is responsible, at least in part, for the curious notion still existing in some quarters that pathology is synonymous with morphology and cannot be more than morbid anatomy. Incidentally, it was not until 1890 that anatomy was separated from physiology in the University of Sydney.

This growth of the medical school demanded additional buildings, and plans were prepared by an architect and Professor Allen. These showed a quadrangle with a large lecture theatre in the front (that is, on the west side), a dissecting room on the north side and a museum of anatomy and pathology on the south side. The museum was to have a wide gallery all round. It was proposed to adopt the style of the old school—a similar Italian portico forming the chief feature. However, it was decided by the Council that there should be a stone frontage of Gothic form. In 1883 (the year in which the first Commencement was held in Wilson Hall) the new building of one story was begun on the present site of the pathology school.

In this year (November, 1883) the collection of pathological specimens formed at the Melbourne Hospital was transferred by deed of gift to the university. This collection, made originally by Dr. Smith and augmented by Dr. Wick and others, was increased so much by the activities of Harry Allen that it had outgrown the storage capacity of the hospital. The only medical school museum was at the back of what is now the physiology school; this later was to become, for a time, the medical school library. Considerable difficulty was experienced in storing the specimens, but this was overcome, and when the new building was completed in 1885 the specimens were transferred to the museum.

The Government had made a special grant of £10,000, but owing to the provision of the more costly Gothic façade it was possible to build only half the proposed museum. As will be seen, the other half was added in 1900. The extent of the first section can be seen in the present

museum, the bolts holding the beams in the old part being different in shape from those in the part which was subsequently added. Despite its reduced size this museum provided satisfactory storage space for the rapidly accumulating specimens, and soon it became famous for both the number and the rarity of some of them.

The museum was Professor Allen's hobby. A friend, calling to see him one Saturday afternoon, found him mounting specimens in the museum. Twenty years ago most of the specimens bore labels in his handwriting. When the method of spending a Saturday afternoon was mentioned he said: "If one day someone obtains as much pleasure from discarding these as I do in arranging them he will be amply rewarded." As they do today, various people desired to view specimens during the week-end and holidays. The possible danger to them was, as it still is,

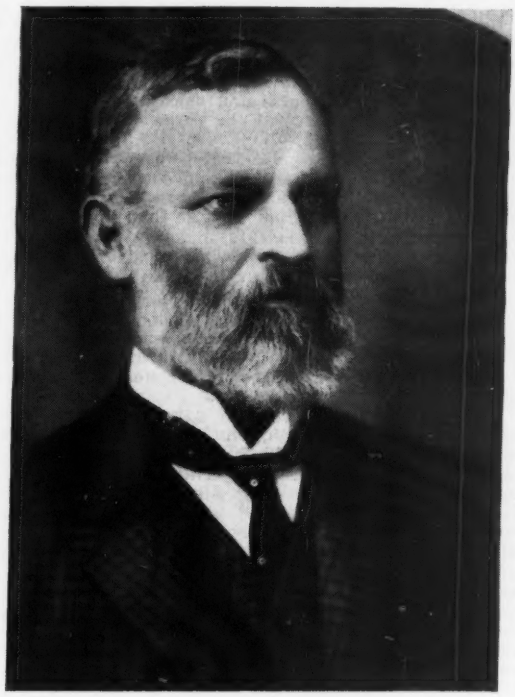

FIGURE I.

Sir Harry Allen, Professor of Descriptive Anatomy and Pathology, University of Melbourne, 1882 to 1906; Professor of Pathology, 1906 to 1924.

obvious. At the same time he did not wish to discourage the enthusiast. So he had a large lock put on the museum door. When a friend exclaimed at the size of the key the professor remarked: "Anyone who does not mind the set of his coat being jeopardized by this key is sufficiently keen to be trusted with it." We are told that there were few who did not quail before its size and prefer to come during working hours.

Another important activity was the formation of a medical school library. Although there may be differences of opinion as to the desirability of its topographical segregation from the main library, there is no question of the far-sightedness of its founders in other respects. Professor Allen was chairman of the library committee, and most of the minutes of meetings were kept by him personally. The old records (preserved in the library) are in his handwriting. The interest in obtaining representative journals is shown by minutes relating to *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* and *Zeigler's Beiträge*. In 1891 it was resolved that the set of *Virchows Archiv* should be completed; apparently only odd copies were available. In 1892 a definite yearly subscription was authorized, but the order for back numbers was countermanded in 1893 (doubtless owing to the depression of 1892-1893); but by 1899 it is obvious that a full set had been obtained. After similar vicissitudes the set of *Zeigler's Beiträge* was completed in 1907. These facts illustrate the manner in which various journals and encyclopædias, which form the backbone of a fine institution, were obtained. At this time the library was housed in a small room behind the physiology department.

In 1886 Professor Allen was elected dean of the Faculty of Medicine. He had taken a leading part in drafting a new curriculum and was largely instrumental in obtaining its acceptance by Council (1887). In 1890 he paid a visit to Europe and made application to the General Council of Medical Education and Registration for recognition of the degrees in medicine and surgery in the University of Melbourne, and he submitted a synopsis of the curriculum. The important point was that the curriculum arranged for a five-year course, despite the recommendation of Professor Paget that it should be only three or four years, and when it was submitted to the Council it made a great impression. Indeed, the president, speaking at the opening of the forty-eighth Session of the Council, said:

> . . . an interesting communication, describing the curriculum and examinations now enforced by the University of Melbourne for its Degrees of Bachelor of Medicine and Bachelor of Surgery . . . might with advantage be sent, together with any recommendations which this Council may adopt, to the several Qualifying Bodies. . . .

It is thus easy to understand that the General Medical Council should have accepted the Melbourne degree for registration.

While Professor Allen was in Europe his duties were performed by Mr. G. A. Syme and Dr. W. Moore in anatomy and by Mr. C. H. Mollison in pathology. In 1884 and 1889 it had been suggested that there should be separate chairs of anatomy and pathology, and in 1891 another attempt to obtain some action was made; but the Government refused to consider the matter. The large amount of teaching — lectures and demonstrations — carried out by Professor Allen now necessitated some assistance. As was mentioned earlier, his demonstrations had been famous; but clearly the large and increasing amount of general work made the continuance of these, in their original form, impossible. Mr. C. H. Mollison had been appointed assistant pathologist to the Melbourne Hospital, where he performed many of the post-mortem examinations, and now Professor Allen encouraged Mr. Thomas Cherry to go to Europe, where he studied pathological histology and bacteriology, especially at Aberdeen.

In 1892 Mr. Cherry was appointed demonstrator of pathology, and for the first time there were systematic classes in pathological histology and bacteriology. There was no laboratory in which these could be held, so they were for some time conducted in Professor Allen's room—an instance of the pioneer's disregard for difficulties. Later gas and water were laid on to the gallery of the museum, and the class was held there for several years. In the same year (1892) a bequest under the will of Dr. J. G. Beaney provided for scholarships in surgery and pathology. More will be said of this later.

In 1893 Dr. Mollison became coroner's surgeon and examiner in forensic medicine. In 1894 Dr. Cherry was appointed assistant lecturer on pathology, a position which he held until 1900. During this period demonstrators in anatomy included such well-known surgeons as John Gordon and Hamilton Russell; but Professor Allen still kept much of the teaching of pathology under his own hand.

In 1897 the Board of Public Health and the Metropolitan Board of Works offered to make annual payments to the bacteriological fund in return for services in the diagnosis of infectious diseases (diphtheria, typhoid and tuberculosis) and regular examination of the Melbourne water

supply. This offer was accepted and was a satisfactory arrangement, in that it supplied sorely needed funds for the developing department, and at the same time it was, and has been since, of great value to the community in general. At first the amount of work was not too great; but as this grew and as the number of students mounted, this service became an increasing burden on the department. In 1899 Dr. R. J. Bull was appointed junior demonstrator to assist Dr. Cherry.

In 1900 additions were made to the pathology department; the museum was completed to its full length and the bacteriology department was built on its present site. In 1902 Dr. Cherry was appointed Government Bacteriologist and in 1905 was made director of agriculture, Dr. Bull becoming lecturer in bacteriology and director.

When Dr. Nield resigned from the lectureship in forensic medicine in 1904, Dr. Crawford Henry Mollison was appointed to this position. "Mollie" occupied a unique position in pathology and forensic medicine in Melbourne. He was born on August 1, 1863, at Bendigo. That his father was a police magistrate may have been partly responsible for his interest in medical jurisprudence. He graduated in 1885 and was demonstrator in anatomy in 1888, and his appointments as coroner's surgeon and assistant pathologist to the Melbourne Hospital have been mentioned. He became pathologist to the Women's Hospital, an honorary but arduous post which he occupied until 1939. He remained pathologist to the Melbourne Hospital, being responsible for the pathological histology until 1928, and indeed he was an active consultant until 1946. His contribution to medical jurisprudence was recognized by his being elected the first medical president of the Medico-Legal Society of Victoria in 1932. He died at the age of eighty-six years. There are many who remember his quiet pleasant smile, the rosy cheeks and the soft voice. In his own unassuming way he did more for pathology here than even his friends appreciated.

Although another unsuccessful attempt was made in 1900 to obtain a separate chair of anatomy, in 1904 a Royal Commission on the university strongly urged the division of the chair of anatomy and pathology. Effective action was taken in 1905, and Professor Allen chose to become professor of pathology. This appointment and that of R. J. A. Berry to the chair of anatomy were made in 1906. It should be noted that a chair of pathology had been formed in Sydney in 1902.

Alterations in the medical school now became necessary. The whole building, except the museum, was carried up into a second story. The old dissecting room (on the site of the present library) became the museum of anatomy. The new room of similar size immediately above it became the dissecting room, and the other rooms of that side of the building were the offices and laboratories of the department of anatomy. The lecture room, which was on the ground floor in the middle part of the building, was transferred to the upper floor and enlarged—this is the present theatre. On the south side on the ground floor (in front of the museum) were offices and laboratories. Above this there was the large laboratory which is still used for pathological histology. These buildings were opened in 1908, and they still retain this form. It may be noted that the stone of the building shows a degeneration of considerable interest to geologists; no doubt it is appropriate that this should be present in the structure of a pathology department. This building shares this degenerative distinction, in Melbourne, with Saint Paul's Cathedral.

From this time pathology began to expand and ramify through the hospitals. As Dr. Cherry and Dr. Bull had become preoccupied with bacteriology, other assistant demonstrators were appointed; these included Dr. Basil Kilvington, Dr. Constance Ellis, Dr. Paul Dane and Dr. C. H. Mollison. In 1908 the Beaney Scholarship replaced the demonstratorships. Dr. S. V. Sewell was the first Beaney scholar and was followed by A. J. Trinca, Gilbert Lamble, Robert Fowler and David Embelton. The Stewart bequest (1909) made possible the establishment of the Stewart lectureship. Gilbert Lamble was the first Stewart lecturer and was followed by Sydney James Campbell and Arthur Wilson.

Gilbert Lamble was in the department for four years, and in 1913 was acting professor, but unfortunately he died in 1917. Dr. Campbell was killed at the landing at Gallipoli.

The importance of clinical pathology in the hospitals began to be appreciated, and Sir James Barrett suggested that clinical pathologists be appointed. At Saint Vincent's Hospital Dr. Andrew Brenan, who was registrar, was appointed part-time clinical pathologist in 1910. At the Alfred Hospital Dr. J. F. McKeddie, who was one of our indomitable pioneers in many fields, had acted as honorary clinical pathologist until 1911, when Mr. A. J. Trinca was appointed full-time clinical pathologist at the princely salary of £100 *per annum*.

The general attitude to ancillary services was shown not only by the salary but by lack of facilities and equipment. There was no microscope with an oil-immersion lens; such an instrument was supplied privately by one of the surgeons. The clinical pathologist performed all post-mortem, histopathological and bacteriological examinations. At first the only biochemical examinations were for free hydrochloric acid and total acidity of gastric juice, and a little later blood urea and blood sugar estimations. A museum was developed at the personal expense of the pathologist.

At the Children's Hospital there was quite a different outcome, owing to the foresight and cooperative action of Dr. A. Jeffreys Wood and the president, Mrs. John Turnbull. A laboratory that was, at that time, a palatial establishment was built in 1913, and in 1914 Dr. Reginald Webster was appointed full-time pathologist—this hospital remaining the pioneer for over a decade.

At the Melbourne Hospital post-mortem examinations were carried out by university demonstrators (Beaney scholars or Stewart lecturers) and by some of the resident staff, and the histopathology was dealt with by Dr. Mollison. It was not until 1929 that a full-time pathologist was appointed.

At New Year, 1914, Professor Allen received a knighthood. He was at the height of his career, so that it is appropriate that we should consider his activities at this point. He had brought a brilliant intellect and a phenomenal memory to bear on all the problems related to medicine and had devoted himself to the building of the medical school in this university. He had been responsible in large measure for the high standard achieved and had ensured that it had become recognized in other parts of the world.

He had played a most important part in matters of general health and medical administration. He was a member of the Central Board of Health in 1883, in 1888 was president of a Royal Commission to inquire into and report on the sanitary state of Melbourne, and in 1889 was president of the Intercolonial Rabbit Commission. He was general secretary of the Intercolonial Medical Congress in 1889, and was president of the combined Medical Society of Victoria and Victorian Branch of the British Medical Association. He was president of the Eighth Australian Medical Congress and a member of the executive committee of the Sixteenth International Medical Congress of 1913.

He had established pathology in Melbourne before the chairs of anatomy and pathology were separated, and his choice of the chair of pathology demonstrated his attachment to this subject. His grasp of pathology was shown by his own work, which was to gain wide recognition, by the standard achieved by his students, and by the museum he left behind him. It has been thought that he overemphasized the importance of syphilis, but this was counterbalanced by the investigations into the Wassermann reaction by Dr. Konrad Hiller (conducted in the bacteriology department in the period 1909 to 1911) and the correlation of results of this investigation with investigations into histopathological changes carried out by Gilbert Lamble. Sir Harry Allen displayed a great interest in these. He kept abreast of advances overseas, though, in retrospect, he was over-influenced by the cell rest theory of Cohnheim (as were many others) and by the endothelial hypothesis (of the nature of many tumours) of

Golgi, Kaufmann, Borst and Zahn. Some of us will remember the vogue of the cylindroma of Billroth. It could be said that his attitude was too rigidly morphological; but morphology was then a new subject—the advancing front of knowledge at the time—and the Teutonic school was in its heyday.

His farsightednes was shown in many ways. Equipment such as the epidiascope and photomicrographic apparatus, obtained in 1912 and used by several departments in the university, was replaced only at the beginning of this year. The development of a medical library has already been mentioned. Outside the university he was largely responsible for the establishment of a School of Tropical Medicine in Queensland. That he was not preoccupied with morphology was shown by the strong support he gave to the development of research laboratories at the Melbourne Hospital, which, in 1916, became the Walter and Eliza Hall Institute. Dr. G. C. Mathison was appointed to direct the laboratories in 1912, but was killed on Gallipoli. The clinical laboratories at the Melbourne Hospital were built in 1914-1916, and Sir Harry Allen was honorary director from their inception as a part of the Walter and Eliza Hall Institute until 1920.

There is a splendour beyond the ordinary in Sir Harry Allen's career. He was typical of the eminent Victorian who understood the secret of service and the joy to be gained simply from labouring in a great cause. He built wisely, providently and spaciously, and his monument is the success that comes from selfless service—here, a school which holds a very high place in the world. "The great difficulty is first to win a reputation; the next, to keep it while you live; and the next, to preserve it after you die." (Benjamin Robert Haydon, "Table Talk".) It is now apparent that all these have been encompassed.

The upheaval caused by the Great War prevented further significant progress for six years and at the same time cast a very heavy burden on some of those who were left to cope with teaching and routine civilian work. Sir Harry Allen played as enthusiastic and strenuous a part in this as he had done in the preceding years. There was one ultimate advantage—the supplies of sera were cut off so that the provision of local supplies became imperative; thus the Commonwealth Serum Laboratories came into being. Dr. W. J. Penfold was appointed first director of the laboratories in 1916, and these were housed on the top floor of the Hall Institute. In 1918 they were transferred to their present site at Parkville.

During the first World War Dr. F. G. Morgan, now Director of the Commonwealth Serum Laboratories, was Stewart lecturer, and for most of the time Mr. Leo Doyle was Beaney scholar. From this stage onwards most of the work at the hospital was carried out by the Stewart lecturer. Clinical pathology did not progress until the end of the war, but now, as was to happen a quarter of a century later, there was (as if to make up for the period of suspended animation) a period of compensatory hyperactivity.

The Walter and Eliza Hall Institute began to function in 1920, with Dr. S. W. Patterson as director and Miss F. E. Williams as bacteriologist and serologist. On Dr. Patterson's resignation in 1923 Dr. C. H. Kellaway was appointed, and under his twenty-one years' directorship the institute established a world-wide reputation. In 1944 Dr. Kellaway resigned (to become director of the Wellcome Institution, London), and Dr. F. M. Burnet was invited to occupy the position.

After the war there were several assistants in the pathology department who not only came to occupy important clinical positions in the city, but retained an interest in pathology. The Beaney scholars were S. O. Cowan, L. B. Cox, D. J. Thomas and Harold Moore. The Stewart lecturers were J. Thomson Tait and Gordon R. Cameron, who is now professor of pathology at University College Hospital, London. In 1920 Frank Longstaff Apperley was appointed lecturer, and in 1923, when the position of senior lecturer was formed, he was appointed to this. Frank Apperley had been a Rhodes scholar in 1910. He was awarded the Armytage and Syme prizes and obtained the degree of doctor of science. He remained as senior lecturer until 1932, when he was appointed professor of pathology at the Medical School of Virginia.

A new anatomy school was completed in 1923 and the anatomy department was transferred to it. The anatomy museum became the medical library, this library being transferred from the totally inadequate rooms at the back of the physiology department. The laboratories in front of this were taken over by the pathology department and the upper floor became the biochemistry department.

At the Melbourne Hospital post-mortem examinations were carried out by members of the staff of the university and by hospital registrars, and the histopathological work by Dr. Mollison, and in 1923 Miss Beryl Splatt was appointed biochemist. There was here a university component to cope with the teaching of students, but at the other hospitals, although considerable teaching was done, there was no real university association.

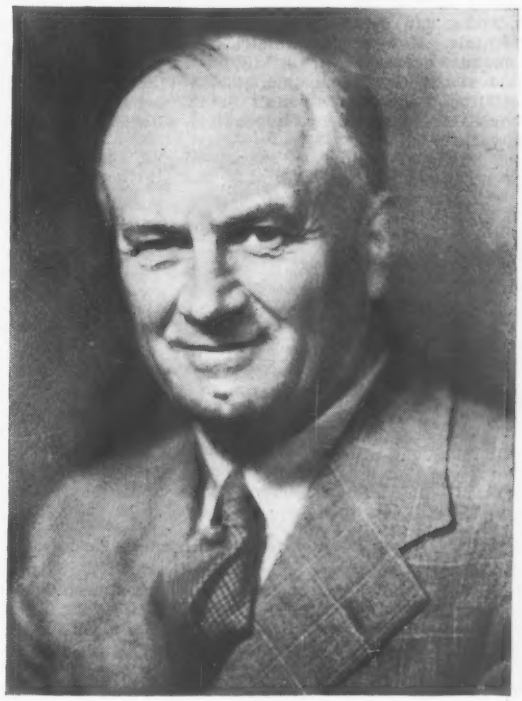

FIGURE II.
Peter MacCallum, Professor of Pathology, University of Melbourne, 1925 to 1950.

Sir Harry Allen now became ill and it was clear that he would not be able to resume his duties, so in 1925 a new appointment was made. Sir Harry Allen died in 1926.

Peter MacCallum came into the school like a breath of fresh air. He infused a life into what had previously been dead. The change that was taking place gradually in other parts of the world was here initiated and animated. There were discussions on life, growth and the importance of the new dynamic embryology. Harry Allen and Peter MacCallum were similar in their capacity for intensive work and in their wide range of interests. Their difference of outlook was due to their belonging to different times—and times change. Probably the greatest personal difference was that Harry Allen was a great individualist, whereas Peter MacCallum had a capacity for attracting and encouraging workers that is given to very few.

Peter MacCallum was born on July 14, 1885, in Glasgow. He lived and was educated in New Zealand and returned

to Edinburgh University. His preliminary training in arts and science determined his outlook on pathology—an outlook which was slowly becoming general, and which was made imperative by advances in knowledge of the subject. To take one example, he emphasized (what was then almost heretical) that a cancer was not something separate from the body, neither autonomous nor a "parasite", but one manifestation of tissue activity and thus part of the body. "The measure of a master is his success in bringing all men around to his opinion twenty years later." (Emerson, "Conduct of Life: Culture.")

He displayed an interest in the practical and clinical side of pathology by holding weekly demonstrations of material (largely operative) at the Melbourne Hospital. He made frequent visits to the other hospitals and personally carried out autopsies in an attempt to bridge the widening gap between the pathology department and the hospitals. However, administrative and extradepartmental demands, as they always will, became great, and at the time of the Bundaberg Commission (1928) these hospital activities ceased. The staff of the department was, of course, too small to cope adequately with the many duties in various places.

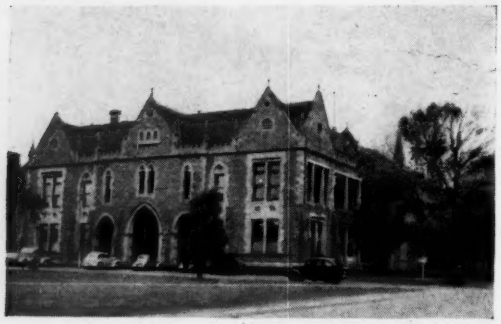

FIGURE III.
Department of Pathology, University of Melbourne.

In 1927 Dr. J. F. Fiddes was appointed as a full-time pathologist to the Alfred Hospital, and in 1928 Dr. R. J. Wright-Smith was appointed to a similar position at the Melbourne Hospital. These were purely hospital appointments and intended to cope with the routine work of the hospital departments; but, owing to the large and increasing number of students, it became essential that the appointees should carry out some teaching. The members of the staff of the pathology department who carried out teaching at the hospitals were appointed assistant pathologists and constituted the only official link in pathology between the hospitals and the university.

Dr. H. A. Woodruff was appointed director of bacteriology in 1929; he was appointed professor in 1935, when the chair was formed. At the Melbourne Hospital in 1929 Dr. Lucy Bryce was appointed as bacteriologist and serologist (she was followed in 1934 by Dr. Hilda Gardner) and immediately began to develop an organization for provision of blood and fluids for intravenous administration; this has gradually developed until it has become the tremendous State-wide Red Cross service that we know today.

In 1931 Dr. R. A. Willis, now professor of pathology at the University of Leeds, became pathologist to the Alfred Hospital, and Dr. L. B. Cox began an investigation of neurological material at the university department and of that at the Alfred Hospital. Dr. Cox was appointed lecturer in neuropathology in 1933, and Dr. Willis gave a course of lectures on tumours from 1935 onwards. In due course other pathologists were invited to act in a similar capacity.

On his return from a visit to Britain and America, Professor MacCallum suggested that a pathological society should be formed in Victoria. A representative group met in Professor MacCallum's room and a constitution was elaborated. The Society of Pathology and Experimental Medicine came into being in 1936. This society has grown and is now probably the most flourishing scientific society in the State.

A large pathological department was now built at the Women's Hospital, and Dr. H. F. Bettinger was appointed as director in 1939. This has developed into an important centre of teaching and research in gynæcological pathology.

The dental students had attended the lectures of the medical course. Since these presupposed a basic training different from what students had actually had, a separate group of lectures and demonstrations was inaugurated in 1940. This clearly allowed a more appropriate and detailed consideration of the subject and has been thoroughly justified by, at least, examination results.

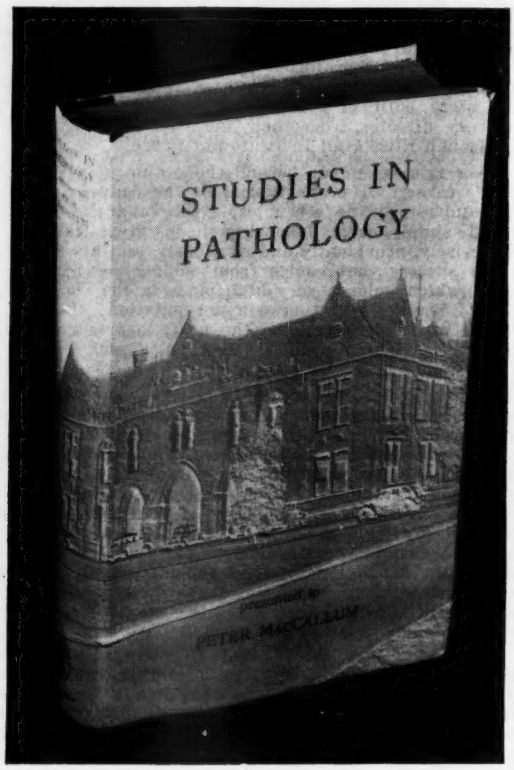

FIGURE IV.
Photograph of the *Festschrift* (in jacket) presented to Professor Peter MacCallum by his students and colleagues in 1950.

With the second World War there was a repetition of the events of a quarter of a century before. Members of the department left Australia with the forces, and one—Dr. Eric Cooper—died on active service. A heavy load was thus again placed on the professor and his small staff, and one cannot overpraise an activity which not only is often overlooked, but which also makes the most stringent demands.

In 1943 Dr. Mollison resigned the lectureship in forensic medicine and Dr. R. J. Wright-Smith was appointed in his place. He held this position until his sudden and unexpected death in 1946. Wright-Smith, born in 1896, a graduate of this university and trained by "Mollie", was an apt successor to him. Most of us remember the stocky figure, the ruddy complexion and iron-grey hair, and many have missed his keen sense of fun and Gargantuan laughter.

Dr. K. M. Bowden was appointed lecturer in forensic medicine and he has done a great deal to bring his department into the front rank. The community has been singularly fortunate in the quality of the men who have held this post, and this is particularly true of the present lecturer; the activities of the Coroner's department have been enhanced by his enthusiasm and single-mindedness.

In the post-war period there was a great increase in the interest displayed toward pathology. The school became crowded with those who had been unable to carry out post-graduate studies and now made up for lost time. The number of students became, as it had done after the first World War, greater than could easily be accommodated.

The number of lecturers and demonstrators increased greatly, to a number that would have astonished our forebears (three senior lecturers, two lecturers, a Stewart lecturer, a dental lecturer, a Beaney scholar and 14 lecturer-demonstrators), and this made it possible to deal adequately with the general teaching. It is important that the number of young graduates, eager to improve their own knowledge, has been sufficient to fill these positions. This is not the time to give details of post-graduate work; but lectures and demonstrations at both the department and the hospitals provided facilities which had never previously been available.

In 1950 Professor MacCallum retired from the chair. The work that he had done for the department, for the university, for the medical profession and for the community (especially on the anti-cancer and tuberculosis committees) had been tremendous. However, his greatest contribution had been in inciting and encouraging activity in members of the staff and his department. Because of this a group of his colleagues and staff produced a *Festschrift* in his honour. The first of its kind to be produced in this university, it is a volume which exemplifies many of the statements made previously, and indeed renders further discussion superfluous.

This brings to a close this all too brief story of the school of pathology. We can visualize the great changes that have occurred if we go back to the last century and see a professor doing all the teaching in anatomy and pathology, writing his notes, letters and minutes of meetings in his own hand, and yet becoming a world figure in pathology. "There were giants on the earth in those days . . . mighty men which were of old, men of renown." Sixty years ago we see him with a demonstrator developing bacteriology and histopathology; then in this century there was the formation of a separate chair of pathology. Even forty years ago there was not a senior lecturer. Then we see the development of hospital routine pathology, teaching and research—tentative at first, but soon becoming robust. The formation of the research institutions was a direct offshoot; but these have grown to such stature as to deserve separate consideration and so cannot be discussed here. In the last two decades there has been an increasingly complex constitution which, from the teaching point of view, as suggested previously, demands some simplification.

Most attention has been given to the two professors. Both have been great men; but we should remember that "Great men are rarely isolated mountain peaks; they are the summits of ranges." (T. W. Higginson, "Atlantic Essays: Plea for Culture.") I think that this at least has been indicated in our story. At the same time it requires individuals to initiate an activity which will produce a harvest of any significance. In the words of Thomas Carlyle ("Heroes and Hero-Worship", Lecture I, Section I):

> All things that we see standing accomplished in the world are properly the outer material result, the practical realization and embodiment of Thoughts that dwell in the Great Men sent into the world.

In this brief and hurried account it might seem that, in the discussion of some of the men, criticism has been implied; if so, it is because "the dwarf sees farther than the giant, when he has the giant's shoulder to mount on". (Samuel Taylor Coleridge, "The Friend", Section I, Essay 8; originally from Richard Burton, "The Anatomy of Melancholy".)

Acknowledgements.

For a considerable amount of the information of early years I am indebted to an unpublished manuscript on "The History of the University of Melbourne", compiled by the following: A. W. Greig, former registrar, University of Melbourne; Leigh Scott, librarian, University of Melbourne; S. S. Addison, former assistant registrar, University of Melbourne.

AN OUTLINE OF THE CONTROL OF NON-SPECIFIC URINARY TRACT INFECTIONS.[1]

By DOUGLAS B. DUFFY, M.S., F.R.C.S.,
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INFECTION of the urinary tract is a common disorder which is handled by general practitioners, physicians and urologists. It is caused by a wide variety of organisms, and a multiplicity of causes may underlie the disease. Thus, in addition to controlling the infection, it behoves those treating this disease adequately to investigate the patient in general, and the genito-urinary tract in particular, before dismissing it as just another "pyelitis" or "cystitis".

One is tempted to neglect this investigation because of the easy administration of and satisfactory immediate results with some of the newer drugs. However, in a proportion of cases this neglect will lead to a recurrence of the infection due to an obvious cause or to the wrong selection of drugs.

I will not discuss the pathology, except to state that most acute and chronic urinary infections are blood-borne, and this is true whether or not there is an obvious cause, such as a renal calculus.

The acute infection is rarely simple pyelitis, but it also involves the renal parenchyma and hence is pyelonephritis. Subsequently the infection may progress to suppuration, may resolve or may become chronic. The chronic stage is important to recognize and treat, because in a proportion of cases the kidney (or kidneys if the condition is bilateral) gradually becomes fibrosed and destroyed, finishing up as a small granular kidney indistinguishable from that of chronic nephritis. In the course of this progression the condition may be the cause of hypertension and finally of renal failure.

The infection may commence as acute pyelonephritis followed by prolonged pyuria, giving rise to frequency of micturition and general ill health, or the acute attacks may recur at intervals, between which the patient feels reasonably well. Sometimes there is no history of an acute infection, but the patient complains of mild urinary symptoms generally over a period of months or years.

Clinically these non-specific infections of the urinary tract fall into two main groups: (i) those in which an adequate cause can be found for the infection, (ii) those in which after thorough investigation no obvious cause is found. It is most important in both groups first of all to identify the infecting organism or organisms, for only by such identification can the correct drug therapy be instituted.

It is worth mentioning at this point that the collection of urine specimens is most important. Specimens passed by females are worse than useless, as they may contain bacteria from vaginal or cervical discharges, and hence a catheter specimen collected in a sterile bottle is essential. From the male a mid-stream specimen is usually sufficient, any prostatic or urethral discharges being washed out in the first portion of urine.

After centrifugation the urinary sediment is submitted to microscopic and cultural examination and the cultured organisms are tested for drug sensitivity. If facilities for culture are not readily available a Gram stain or simple stain with methyl violet is of great assistance, as it will

[1] The substance of a paper read at the annual meeting of the Royal Melbourne Hospital Old Students' Association in March, 1950.

at least tell one whether the organism is a coccus or a bacillus. This is of value in selecting the appropriate drug, because the bulk of urinary tract infections are due to Gram-negative bacilli which are not sensitive to penicillin.

A thorough urological investigation, including excretion pyelography and cystoscopy, is then instituted to find a cause for the infection. A good excretion pyelogram will reveal any upper tract disease, such as congenital abnormalities, hydronephrosis, stone, tumours *et cetera*. If indicated, retrograde pyelography is carried out. Cystoscopic examination will reveal any bladder abnormality, such as diverticulum, tumours *et cetera*. If there is any suggestion of bladder-neck obstruction, particularly in men aged over forty years, this region should be carefully examined with the panendoscope. One sees a number of men with recurrent urinary infections who have been fairly thoroughly investigated, but who have a bladder-neck obstruction such as fibrous bar, which has not been found because it can be properly visualized only by panendoscopic examination.

One must be particularly careful in diagnosing cystitis in people aged over forty years, because an attack of cystitis or recurrent cystitis may be the first manifestation of a carcinoma of the bladder, and all these patients should be cystoscopically examined. Even on cystoscopic examination it may be difficult at times to distinguish between cystitis and carcinoma of the bladder, and if there is any doubt a biopsy should be taken with the resectoscope.

Once a cause has been found, correct treatment of this cause together with the correct drug therapy will usually clear up the infection. However, there remains a large group of patients, particularly females, in whom no cause can be located. In such cases sources of infection outside the urinary tract, such as infected teeth, tonsils, gall-bladder *et cetera*, must be sought. The removal of such a focus will occasionally be attended by great success as far as clearing the urinary infection is concerned, but unfortunately this is the exception and not the rule.

In a large proportion of cases no cause can be found, and so the infecting organism itself must be treated alone.

The importance of eradicating urinary tract infections is underlined by the tremendous amount of ill health and chronic disability which they cause, and by the fact that a proportion of these patients will die of chronic renal failure due to their disease.

Before urinary antiseptics are prescribed it is important to determine the adequacy of renal function. Extensive disease of the kidneys will not only cause them to fail to concentrate the drug in the urine in sufficient amounts to eradicate the infection, but may lead to toxic concentrations of the drug in the blood-stream and body tissues. A urea concentration excretion test together with the excretion pyelogram prepared during the investigations will give all the information that is necessary.

The relative percentage of different organisms in urinary tract infections varies from series to series; but roughly 80% to 85% of infections are due to Gram-negative bacilli and 15% to 20% are due to Gram-positive cocci—staphylococci and streptococci. Of the Gram-negative organisms, *Escherichia coli* is the most common by far, and is followed by *Pseudomonas pyocyanea*, *Aerobacter aerogenes*, *Escherichia intermedium*, *Proteus*, *Alcaligenes* and the paracolon bacillus. Some of these are differentiated only by special bacteriological tests, and if these tests are not performed the organisms may be reported as *Escherichia coli*. This sometimes explains the resistance to drug therapy of an organism which we think is *Escherichia coli*, whereas in reality it is *Escherichia intermedium* or *Aerobacter aerogenes*.

Now let us consider the drugs available to deal with these various organisms. Chemotherapy in urinary tract infections dates back only to 1930, when the ketogenic diet was introduced by Clark and Helmholtz. This rather cumbersome method of bacteriostasis by acidification was replaced when Rosenheim introduced mandelic acid therapy in 1935. Mandelic acid is given in divided doses, up to eight to twelve grammes per day. Fluid intake is restricted to 1000 to 1500 millilitres per day, and the urinary pH is tested daily and must be kept below 5·5. It is best tested with nitrazine paper and colorimeter charts. The duration of treatment is eight to twelve days, and courses may be repeated at intervals. Mandelic acid is given with ammonium chloride to acidify the urine, unless, as is now usually done, ammonium mandelate is used. This is put up in a syrup as a 40% solution, and the average dose is two drachms of 40% solution four times per day—a total of 12 grammes. The patient is cautioned against taking such things as fruit juices, which render the urine alkaline. Mandelic acid therapy has the disadvantage of fluid limitation if the patient is febrile and is contra-indicated if renal function is poor. Nausea can usually be controlled by giving the drug after meals.

Mandelic acid is extremely effective against *Escherichia coli* and *Streptococcus fæcalis*, but is of no value if the organism is a urea splitter, as in these cases it is impossible to acidify the urine. Urea-splitting organisms such as *Proteus vulgaris* and some staphylococci and streptococci are of great importance in stone formation, as they split urea-forming ammonia, which then combines with phosphates and carbonates to give triple phosphates. Infections of the last group frequently penetrate deeply into the tissues and often produce ulcerations and incrustations. Their presence together with renal calculi is a bad prognostic omen, as their eradication is difficult, and recurrence of the stones after surgical removal is frequent.

Treatment with hexamine, which depends for its action on the liberation of formaldehyde in an acid medium, and alkalinization of the urine by means of potassium citrate, are two other methods which are used to control urinary infections. They will control a proportion of uncomplicated *Escherichia coli* infections, but their usefulness is limited and we have much better drugs at hand.

The sulphonamides, which were next introduced, are effective over a fairly wide range of organisms, particularly against streptococci and *Escherichia coli*—they cure about 60% of the latter infections. They are active in an alkaline medium, unlike mandelic acid, and are occasionally, although not often, useful against *Proteus vulgaris*. They have little value in infections due to *Streptococcus fæcalis*. Dosage is not large, as the urinary concentration is 10 to 20 times that of the blood, and three to six grammes per day are sufficient. All the different sulphonamides have slightly varying effects on different organisms, but sulphadiazine is as generally useful as any. Combinations of sulphonamides such as "Sulphatriad" are widely used, on the basis that there is less danger of crystallization with the lower concentrations of each individual sulphonamide, while a high total sulphonamide concentration is maintained. It seems doubtful whether this is borne out in practice. All sulphonamides occasionally give complications, such as nausea, rashes, fever, hæmaturia and anuria. If hæmaturia develops, the drug should be discontinued immediately and intake of fluid forced. Should anuria occur during sulphonamide therapy, it may be obstructive in nature, from actual blocking of tubules, pelves or ureters by crystals, or it may be due to tubular damage—lower nephron nephrosis—or to a combination of both of these causes. The clinical differentiation of these two types of anuria is difficult, and cystoscopic examination with ureteral catheterization is performed as soon as possible, the kidney pelves being irrigated with alkaline fluid to wash out any obstructing crystals. Should the anuria be due to tubular damage, nothing but harm can be done by forcing fluid intake and giving diuretics. Fluid intake should be restricted to the amount lost by insensible perspiration and any vomiting, and should not exceed 600 to 1000 millilitres per day. If the tubules are capable of recovery they will do so within a period of about ten days, and during this period we should aim to keep the patient's electrolyte balance as nearly normal as possible and avoid drowning him with fluids.

The urinary complications can be minimized by not giving large doses, by a liberal fluid intake and by giving alkalis with the drug. Administration of all these drugs should be continued until the urine has been clear for four to five days and two or three negative cultural results have been obtained.

"Mandelamine" is a useful drug which is formed by the union of mandelic acid and methenamine (hexamine). It is given in tablet form—three tablets four to five times per day—with no restrictions in diet or fluid intake. Mandelamine is very useful in that it is non-toxic and can be given to ambulatory patients with good results in *Escherichia coli* infections. It eradicates 80% of *Escherichia coli* infections, but is not of much use against *Proteus* or *Aerobacter aerogenes*.

Penicillin is not of great value in urinary tract infections, except when the organisms are staphylococci or streptococci, when it certainly is the drug of choice. As the majority of infections are due to Gram-negative organisms, penicillin is often given quite uselessly. It is rapidly excreted in the urine, in which it has a high concentration, and is now most conveniently given as procaine penicillin, 300,000 units daily, although any of the other recognized methods of giving the watery solution are satisfactory.

Streptomycin, discovered by Waksman in 1944, must be given parenterally, as it is not absorbed from the gastro-intestinal tract. A large percentage of the drug is excreted in the urine in twelve hours, and a high urinary concentration can be maintained by giving one or two grammes per day in divided doses.

Escherichia coli is sensitive to streptomycin in 95% of cases, and generally it is the most satisfactory drug for use against this organism. If the infection does not clear within a few days the organisms rapidly develop a fastness to the drug, and it is useless prolonging treatment with streptomycin. *Proteus* is an important organism which is sensitive to streptomycin in about 60% to 70% of cases, streptomycin being active in an alkaline medium. *Pseudomonas pyocyanea* is resistant in a high proportion of cases, and other Gram-negative organisms are sensitive in proportions varying between 20% and 40%, and so it may be worth trying. *Streptococcus fæcalis* is not sensitive.

There may be great variation in the response of different strains of the same organism to streptomycin, and sensitivity tests *in vitro* are not always a true indication of its action *in vivo*. The toxic effects, such as pain on injection, nausea, tinnitus and vertigo, due to eighth nerve damage, are well known.

Aureomycin is put up in 250-milligramme capsules, and the dosage is two capsules every six hours, given by mouth. It is unstable and is not put up in solution. Aureomycin is particularly effective against *Escherichia coli* and *Streptococcus fæcalis*, hence it may be of use in streptomycin-resistant *Escherichia coli* infections.

Proteus and *Pseudomonas* are not sensitive, but some of the other Gram-negative organisms are moderately susceptible. Toxicity is low, and nausea can be avoided by giving "Amphogel" with the capsules. Aureomycin is said to be effective in Reiter's syndrome, for which arsenic given intravenously is usually, but not always, curative.

"Chloromycetin" is an antibiotic given by mouth in doses of 50 milligrammes per kilogram of body weight, the average daily dose being in the region of 2000 to 3000 milligrammes. It is particularly effective against *Escherichia coli* and has given moderately good results against *Pseudomonas pyocyanea*. On the other Gram-negative bacilli its effect is variable and not outstanding.

Finally, there is "Gantrisin", or NU 445, a new sulphonamide which is being used in America and should be available here soon. It does not require alkali therapy, as it is highly soluble in an acid medium, and therefore there is no apparent danger of crystalluria. It can be given orally or intravenously in the same dosage as the other sulphonamides. *Proteus* is sensitive to "Gantrisin", and if it does help to combat this organism it will be a great help. Other Gram-negative organisms are only mildly sensitive.

Many urinary tract infections are caused by a mixture of different organisms, and a combination of drugs may have to be used or a series of drugs tried in an effort to control them. Failure to remove the infection may require drugs to be changed as organisms become resistant. Complete eradication of infection in some cases is almost impossible or, if it is obtained, relapse occurs soon after discontinuance of therapy. In these cases small maintenance doses of sulphonamides or intermittent doses of mandelic acid may control the infection and keep the patient comfortable, even if some infection still remains.

Conclusion.

In conclusion I would like to stress three points: (i) search for a cause for the infection; (ii) carefully isolate and examine bacteriologically the organisms causing the infection; (iii) use the appropriate drug according to the organism isolated.

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POLYCYSTIC DISEASE OF THE KIDNEYS.

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J. D. FERGUSSON (1949) quotes figures for the incidence of polycystic disease of the kidneys as found at autopsy. These vary from 1 in 1019 at the Mayo Clinic to 1 in 428 in New York, 1 in 250 in Leningrad, 1 in 242 in Boston and 1 in 158 in the Jewish Hospital, Brooklyn. The incidence was 1 in 356 in a collected series of 23,900 autopsies collected by Davis.

Our method of tabulating the summaries of post-mortem examinations 1000 at a time and publishing them in *The Medical and Scientific Archives of the Royal Adelaide Hospital* enables a quick review to be made of any particular pathological condition. Thus in the 7000 tabulated post-mortem examinations made between 1920 and 1948, there were 28 examples of polycystic disease of the kidneys, or 4 per 1000 (1 in 250). The figures for successive thousands were 5, 5, 1, 5, 9, 1 and 2—a total of 28; thus a good deal of variation was shown, as might be expected by chance.

Twenty instances were in males and eight in women. As the autopsies on men were about twice as many as on women, these figures do not indicate any definite preponderance in one sex. Of the males, three were in the thirties, three in the forties, seven in the fifties, five in the sixties, and two in the seventies, the youngest subjects being two men aged thirty-four years, and the oldest a man aged seventy-eight years. Of the women, one was aged eighteen years, one thirty-nine years, there were five in th forties and the oldest was aged seventy years. Nine of the 28, consisting of six men and three women, died from their polycystic disease alone or with superadded fibrotic

changes in the kidneys, probably in all the cases from uræmia. The male subjects comprised the following: (i) A man, aged forty years. (ii) A man, aged fifty years, with uræmia; the kidneys weighed 133 and 110 ounces respectively, and the cystic liver 96 ounces. (iii) A man, aged fifty-six years. (iv) A man, aged fifty-nine years, with uræmia and hæmorrhagic pericarditis; the kidneys weighed 64 and 46 ounces respectively. (v) A man, aged sixty-eight years, with superadded chronic nephritis and uræmia; the kidneys weighed 7 and 10 ounces respectively, the polycystic liver 70·5 ounces. (vi) A man, aged seventy-eight years, the oldest subject; the kidneys were not large and he also had silicosis and tuberculosis.

The three female subjects comprised the following: (i) A woman, aged thirty-nine years; the kidneys measured ten by six by two inches. (ii) A woman, aged forty-three years, with uræmia; cysts were present also in the liver. (iii) A woman, aged forty-three years, with uræmia and small cysts in the liver.

Six of the 28 died from cerebral, pontine or cerebellar hæmorrhage, only two from carcinoma (elsewhere). Other various causes of death were aortic stenosis, subdural hæmorrhage after a blow, *Clostridium welchii* infection after abortion, bacterial endocarditis *et cetera*. The occurrence of six cases of hæmorrhage in the brain may perhaps have had some connexion with the polycystic kidneys, but if so one would have expected some deaths to follow hypertension manifested by an hypertrophied heart which had failed, and these were absent.

In some of the examples the kidneys were not much enlarged, and sometimes it was difficult to decide whether one was dealing with kidneys with an unusual number of microcysts (which are often present in the somewhat fibrosed kidneys of elderly persons), or with mild examples of polycystic disease. The largest kidneys weighed 133 and 110 ounces (3773 and 3120 grammes), 64 and 46 ounces (1815 and 1305 grammes), 35 and 24 ounces (993 and 681 grammes), 20½ and 19 ounces (560 and 539 grammes), and 20 and 19 ounces (568 and 539 grammes). In another case the size of the kidney was 10 by 6 by 2 inches (25 by 15 by 5 centimetres), and in another "half the size of a football".

Cysts in the liver, hall-marking such cases, were present in eight and were usually small in number and sometimes few. One affected liver weighed 122 ounces (3460 grammes), another 96 ounces (2723 grammes) and another 70·5 ounces (2000 grammes).

In the pathological museum of the University of Adelaide are two good examples of the great size that polycystic kidneys may reach. The first to be quoted is also of interest as showing that, in spite of the very large size (and one would imagine some pressure atrophy of the healthy renal parenchyma), and even with surgical removal of one kidney, the patient may live long enough to die from something quite unconnected with the kidneys. This patient was a man, aged thirty-three years at the time of death, whose kidney had been shown at a meeting of the South Australian Branch of the British Medical Association on November 30, 1905, by Dr. W. A. Giles, fourteen days after it had been removed on account of intestinal obstruction. He was then aged twenty-six years and had subsequently returned to work in the smelters at Port Pirie and had been passed as a "first-class life". Two years after operation he appeared to be in the best of health, but in 1911 he died of pneumonia and meningitis. Both kidneys were enormously enlarged, with irregular knobby surfaces, the left measuring approximately 25 by 14 by 12 centimetres, the right 25 by 13 by 10 centimetres, and they were made up of a very large number of cysts ranging in size from that of a shot to about six centimetres in diameter, with fibrous walls of varying thickness and here and there small areas of renal tissue wedged in between the cysts. The contents of the latter were chiefly watery fluid, but a few contained a semi-gelatinous colloid material.

The second example is from a man, aged forty-eight years, who died from cerebral hæmorrhage on July 16, 1891. The right kidney weighed six pounds (2723 grammes) and the left five pounds (2269 grammes). There were also several smooth-walled cysts in the liver. This at the time was thought to be a record case as regards the age of the patient at the time of death.

Summary.

1. The incidence of polycystic kidneys in South Australia, based on 7000 autopsies, is about 1 in 250 (varying from 1 in 1000 to 9 in 1000).

2. Nine of the 28 patients died, probably from uræmia, as a result of having this condition, and six others from hæmorrhage in the brain, which might indirectly have been due in part to the effects of the polycystic kidneys.

3. As more examples were found among persons who died in their fifties and sixties than in their thirties and forties, the inference may be made that in many cases, at least of minor instances of the condition, the patient may live to a good age and die from some other cause.

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ENURESIS AND TOILET TRAINING.

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AND

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INTRACTABILITY of a disease is often due to ignorance of its ætiology. Enuresis falls into this category. Its notorious stubbornness to treatment and its serious sequelæ make it worthy of close study.

The frequency can be gauged from the figures of Edna Hill (1949), who reported no less than 133 enuretics out of 462 normal pre-school children. Enuretics are so common in child guidance centres and in general medical practice as to create a therapeutic problem of considerable magnitude.

Whilst a concept of disharmony in the sympathetico-autonomic system controlling the bladder can be cited as descriptive for ætiology, the ultimate causation is obscure. Enuresis occurs with monotonous regularity in apparently well-regulated families, and may be entirely absent in many from the most ignorant strata of society. There is no common underlying physiological factor.

The variety of treatments employed is so great as to arouse considerable suspicion of our ignorance. One must confess that the treatment of an enuretic commences in such an atmosphere of doubt as to militate against the certainty of success.

Previous observations on pant-wetting outlined in the department of medical psychology (Bostock and Hill, 1949) suggested the need for further research. The present communication deals with the relationship of enuresis to breast feeding and toilet training.

Case Material.

For the purpose of this inquiry a survey of methods and attitudes adopted during breast feeding and toilet training of children up to five years was conducted at a Brisbane kindergarten. Seventy-three mothers of children were interviewed by one of us (M.G.S.). The mothers were previously warned by the director of the psychologist's visit and were invited to cooperate in an important investigation. The appointments were made individually and were arranged through the director.

The forty-minute interviews were carefully planned so as to elicit a description of the breast-feeding and toilet-training technique, domestic happiness and psychological implications to the child. Questions were so framed as

to convey the minimum of suggestion. Care was taken to impress each mother with the secrecy and importance of the interview. Fortunately the psychologist was herself a mother. This improved the *rapport*, which was highly satisfactory.

As the interview progressed and the interviewer maintained an attitude of interest and neutrality, the women almost without exception spoke not only volubly but feelingly about their problems and convictions in regard to the handling of the baby during the first twelve months.

The comprehensive inquiry was steered through reminiscences, complaints, regrets and convictions until the mother came to the crux of her emotional life. She told her enjoyment of the physical contact of breast feeding and of her impatience and annoyance when holding a small baby out over a trainer; she discussed the planned baby, the accidental baby, the unwanted baby, and the marital bliss or otherwise she enjoyed during pregnancy and lactation. In all these matters the women were generously frank.

The parent's estimate of personality deviations in the children was compared and checked with the case records of the kindergarten and with the observations of the director herself.

Breast Feeding.

The primal pattern of a baby's security occurs when the mother's breast is freely and lovingly placed at his disposal. This is of inestimable value as setting the template for future behaviour. In view of current emphasis concerning the relationship of early security as a background for enuresis, it was felt that the pattern of breast feeding might play a part in its genesis.

The following data show that whilst the type of breast feeding is not the direct cause there are important implications.

Domestic Happiness.

Domestic happiness is apparently a first prerequisite to successful lactation.

Among our 73 mothers 12 reported grave marital disharmony. Of these, 10 admitted that breast feeding was an unpleasant duty. Of the remaining 61 happily married mothers, 22 only admitted to disliking breast feeding.

When these figures are viewed statistically, the association which tends to exist between domestic happiness and a satisfactory emotional attitude towards breast feeding is very highly significant (the χ^2 probability is 14·6).

The findings are undoubtedly of interest to the prospective mother. Often in her search for an adequate preparation to lactation she over-stresses diet and vitamins. When the doctor is asked for advice concerning the care of the breasts during pregnancy, he must not neglect to inform her that contentment of mind and a state of domestic harmony are equally important.

That certain personality traits are influenced by the type of breast feeding is evident from the following figures.

Aggressive, Destructive and Stubborn ("A.D.S.") Impulses.

Our records show that of the 73 mothers, 41 admitted to enjoyment of breast feeding. Of their children, only seven were reported as having "A.D.S." to a pronounced degree.

The remaining 32 mothers found breast feeding disgusting, or at least unpleasant. Of their children 13 were described as having "A.D.S." impulses to a pronounced degree.

Submitted to χ^2 analysis the association which tends to exist between the occurrence of "A.D.S." traits and an unsatisfactory maternal attitude to breast feeding is significant (the χ^2 probability is 5·7).

When the mother is emotionally cooperative and the milk is given ungrudgingly and with pleasure, then the child tends to be free of aggressive, destructive and stubborn impulses.

This finding has been frequently confirmed by others.

The same direct correlation with personality deviation is not found in the genesis of enuresis.

Breast Feeding and Enuresis.

As stated above, 41 children were fed in association with satisfactory maternal attitudes. The remainder (32) had an unsatisfactory nurture. Among the former, 16 cases of enuresis occurred, while 13 were found among the latter.

The standard for considering a child as an enuretic was the passing of urine involuntarily during sleep into the bed at least three times per week. Many were offenders on every night of the week. The occasional bed-wetter was not included in our list of enuretics.

The total (29) was made up of 16 boys and 13 girls. This is out of a total of 37 boys and 36 girls investigated.

The χ^2 probability of a direct relationship between enuresis and type of breast feeding is 0·5. This is statistically insignificant.

Whilst, therefore, no type of breast feeding can be identified with the subsequent development of enuresis, there is a common factor in the importance of maternal affection and emotional harmony. This will be discussed later.

Toilet Training.

The part which toilet training plays in enuresis will now be considered.

Of our 73 children, 43 were toilet trained with impatience, often verging on cruelty; the routine was enforced and rigid; 26 are enuretics.

Among the remaining 30 children who were trained without coercion, three have enuresis.

There is therefore a definite association between enuresis and a rigid toilet training. (This is shown by the χ^2 probability of 18·4).

The rationale of this finding will now be discussed. It would seem to fit into the framework of a conception of enuresis as the end product of a total situation.

Enuresis cannot be regarded as a single phenomenon. In the past we have tended to look on it as an annoying symptom for which the remedy is a drug, a diet or a psychological *tour de force*. On the contrary, enuresis has its roots in the total personality of the child, and this includes the whole attitude of the parent to the child from the moment that breast feeding and toilet training commence.

General Considerations.

The clue to the precise relationship of enuresis to toilet training is suggested by figures concerning the unwanted child. In our total of 73 children, 26 were unwanted. Of these, 18 were rigidly toilet trained. Among the 47 children who were wanted, 20 had rigid toilet training. The χ^2 probability of there being a relationship existing between the wanting or otherwise of children and the casual or rigid toilet training of them is 4·4. This is significant.

Let us now consider the psychology of the mother of the unwanted child. There is an unfortunate and disastrous repercussion. She appreciates her failure in love and over-compensates by her intense urge to produce a wonderful child. She commences her task as soon as possible. The first step is the perfect performance on the pot, and a prompt emergence from the diaper existence. Furthermore, the beastly diaper is a constant reminder of her unwanted slavery. She has a legitimate reason for wishing to terminate its use as soon as possible. To the above end progress is daily assessed on the time factor in defæcation and the lessening daily average in nappies. The fussy, zealous, perfectionist-minded matron dazzles us with her energy, devotion and attention, but she is merely using these as a façade to conceal the hollowness of her own emotions. She has an unwanted child; she insists that it shall be perfect, and, alas for the frailty of human wishes, she insists on driving it along the road to enuresis.

The figures for the incidence of enuresis among wanted and unwanted children are as follows. Of 37 wanted children, 10 were enuretic and 27 non-enuretic; of 26 unwanted children, 19 were enuretic and seven non-enuretic.

The χ^2 probability of relationship between a child's being unwanted and subsequent enuresis is here 15·9, which is very highly significant.

But, as we have seen, not all enuretics are unwanted.

It is apparent that others factors are operative in the choice of toilet training methods adopted by some "happy" mothers. Their own early upbringing may have laid down patterns of compulsive cleanliness; they may have to contend with the standards maintained by perfectionist friends or trained advisers. Often adherence to the letter of advice rather than to the spirit of the instruction is observed.

Spurred to achieve early a high degree of toilet cleanliness, such a mother frets herself and harasses her baby until the one is irritable and the other frightened. Toilet training is achieved—the habit is punctual and regular and the training is completed possibly before the end of the first year.

The later development of enuresis depends largely upon the degree of later frustration to which the toddler will be subjected, but the mother has created the necessary predisposition.

It seems to us that the same end point of a rigid perfectionist training routine can be reached along two different routes. The "unwanting" mother over-compensates, whilst the "wanting" mother is subject to persuasion, suggestion and imitation.

Affectionate mothers are often drawn along the perfectionist path by the modern glamorized efforts of enthusiastic baby trainers. Whilst it is true that the efforts of such reformers as Truby King *et alii* have saved many lives, they have committed many psychological errors. The reader is referred to a communication by James L. Halliday (1946). He describes the profound changes found in the *milieu* of infancy from 1860 to 1930, in accordance with the principles of up-to-date scientific physical hygiene, and states that nothing resembling it has been found in the previous history of man. He contrasts the natural unfolding of life prior to this system with the regimentation of bowel-training. "When the clock struck certain hours 'little pots were punctually applied to little bots'."

It seems to us that the time of toilet training, whether before or after weaning, is immaterial. The accent must be placed upon the manner of its performance. It should be so kindly and smooth that no tensions arise. There must be no rules involved. The sanctity of the clock and the high altar of sacrificial devotion to the pot must alike become the forgotten trappings of an outworn cult.

Hadfield (1950), in dealing with the cultivation of conditioned habits, remarks that as a feed of milk produces a movement of the bowels in the infant, the sensation of being put on a pot at that time will thereafter act as a conditioned stimulus and produce a motion even in the absence of feeding.

This is very different from the type of toilet training which runs life by the clock and makes eating, sleeping and defæcation occur on a time basis and not on a needs basis.

The cynic might remark that if Nature had wished us to run our lives by the clock she would have given us a stop-watch in our heads!

The late Susan Isaacs (1935) has pointed out that the modern mother is asked to chase artificial norms. "Spurious standards as to the normal age of sphincter control are often taught in a way that makes mothers unnecessarily upset by the difficulties occurring so commonly in the years following infancy." In other words, theoretical norms are regarded as "musts" to be attained by all. Unfortunately such high standards force over-stimulation and the production of anxieties.

Norman R. F. Maier (1949) has approached the problem from another angle. He presumes that frustration produces enuresis. In this respect it would be hard to imagine a more frustrating life than that entailing frequent coerced visits to a cold and disagreeable pot, which gives neither satisfaction nor security. He states: "If the insecure, enuretic child is given excessive love and attention and his bed-wetting is overlooked he is more likely to be cured than if a direct approach is made to correct the enuresis."

Our clinical experience is in agreement with the above finding. It leads us to a consideration of why the child who has acquired toilet cleanliness under rigid training breaks down and becomes enuretic. Habits learned under frustration are not stable, but tend to disintegrate with the continuance of frustration. The reason is that the conditioning is linked with the discomforts of frustration. In some cases it is also linked with fear. When frustration and fear are again experienced there is a tendency for regression to occur. Bed-wetting appears, and habits of cleanliness have to be relearned. Unfortunately the secondary frustration introduces new characteristics. The behaviour is less subject to the influence of rewards and punishment and more stubborn to eradicate, and any change is apt to be regressive or hostile.

Maier (1949) has shown by experiment that habits learned under frustration tend to disintegrate with further frustration, and in this process stereotypies appear. These may be based on some phase of an original habit. Thus, whilst rigid toilet training produces an initial habit of cleanliness, the habit is unstable and may break down to produce stereotypies under continued frustration. A stereotypy is a fixation which is peculiarly strong and persistent. It serves no useful function, and is not susceptible to the influence of rewards and punishments. The enuretic act is a clinical stereotypy. This accounts for the extreme difficulties in treatment.

A simple illustration of stereotypy is seen in swearing. The child is laboriously taught to use clean speech, but when a frustrating incident occurs the swear "stereotypy" appears.

It may be asked why frustration leads to release of urine as a stereotypy rather than of fæces. This is probably due to "availability". The act of defæcation is less susceptible to control by the higher centres than that of micturition.

The above process may be summarized thus:

First Phase of Initial Accomplishment: Rigid training, frustration and possibly fear = conditioning and habit = early toilet mastery.

Second Phase—Failure: Frustration and possibly fear = habit disintegrates = regression and stereotypy (enuresis).

Prognosis, Prophylaxis and Treatment.

The relationship between rigid toilet training and enuresis has far-reaching implications in prophylaxis and treatment. With regard to the former, if an observer knew the degree of maternal love, the degree of domestic harmony and the type of toilet training, he could make a shrewd prognosis on the future presence of enuresis.

Conversely, if a parent wishes to ensure that his child will not belong to the legion of bed-wetters, he will know that the correct psychological approach to the above basic factors will favour the desired goal.

The correct treatment of the enuretic depends upon the discovery of causation. Encouraging results have been achieved by us through the removal of frustrating factors. This will form the subject of a further communication. Investigation of enuretics at the Child Guidance Clinic of the Children's Hospital in Brisbane confirms the theses outlined above. This is shown by a series of 25 enuretics, of whom no fewer than 23 had been toilet-trained on rigid lines.

Crosby (1950) has recently successfully treated enuretics with an ingenious apparatus designed to rouse the patient from sleep at the onset of micturition. Although he uses a mechanical contrivance, there is a sound psychological implication in the process. The patient is made to feel secure and is so guided towards the desired goal of a dry bed.

His results in no way conflict with the underlying psychology upon which the above thesis rests.

Summary.

1. The relation of breast feeding and toilet training to later enuresis is explored.

2. No significant association with breast feeding is discovered.

3. Rigid toilet training is found to be strongly associated with later enuresis (the χ^2 probability is 18·4).

4. A significant association is found between the type of toilet training and acceptance of the child. Unwanted children tend to be rigidly trained.

5. The frustration factor in breaking down habit formation is discussed.

6. The importance of the above findings in prophylaxis and treatment of enuresis is stressed.

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PRIMARY GLAUCOMA.

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THERE are two distinct types of primary glaucoma. In the first group crowding of the angle of the anterior chamber is the cause of the raised intraocular pressure. In the second group interference with the absorption of aqueous from the region of Schlemm's canal appears to be the chief factor.

The first group is called "congestive" or "narrow-angle" primary glaucoma; "narrow-angle" is the admissible term, because these patients always have a shallow anterior chamber with a narrow entrance to its angle. However, "congestive" primary glaucoma is not a good term, as many cases in this group run a chronic course without any noticeable congestion.

The second group is referred to as "non-congestive", "chronic simple" or "wide-angle" primary glaucoma. "Wide-angle" is not a good term, because this type of primary glaucoma occurs in eyes with anterior chambers of any depth and with angle entrances of all widths. "Non-congestive" is likewise not an accurate description of the group, because congestive attacks can occur in two instances: (*a*) when the patient is born with a shallow anterior chamber and a narrow-angle entrance and subsequently develops this second type of glaucoma; (*b*) in advanced stages, when anterior peripheral synechiæ have formed.

"Angle crowding" and "non-angle crowding" are terms which would draw attention to the basic causative factors in the majority of cases in the two groups; but they have the same misleading disadvantages as "narrow-angle" and "wide-angle", "congestive" and "non-congestive".

CLASSIFICATION OF PRIMARY GLAUCOMA.

Primary glaucoma may be classified as follows:

Type I.
- (*a*) Acute congestive.
- (*b*) Chronic narrow-angle.

Type II.

Rare Types.
- Low-tension glaucoma.
- Reece's rare type II.
- Intermittent glaucoma.
- Pseudoglaucoma.

Intermittent glaucoma and pseudoglaucoma are not really primary glaucomata; but it is not intended to discuss here any of the rare types mentioned above.

Type I Primary Glaucoma.

Patients with type I primary glaucoma always have a shallow anterior chamber and narrow-angle entrance, and the majority have signs and symptoms of corneal œdema. Treatment consists in prompt surgical measures. The best provocative test is the dark-room test, which often enables the surgeon to make a diagnosis in the pre-glaucomatous stage.

Kronfeld states that a narrow-angle entrance with either a history of corneal œdema or a positive response to the provocative test (dark room) means type I glaucoma; I do not entirely agree with this view. A narrow-angle entrance and a positive response to the dark-room provocative test is correct; but a history of corneal œdema *plus* a narrow-angle entrance and a negative response to the provocative test is insufficient for a diagnosis of pre-glaucoma type I primary glaucoma, and operation is not indicated in these latter cases.

In America it is stated that in 80% of eyes with narrow-angle entrances, type I glaucoma develops within five years in people aged over forty years. At a meeting of the Ophthalmological Society of New South Wales the unanimous opinion of the members was that this figure is far too high, at any rate for the Australian population.

For years broad iridectomy has been used successfully in the treatment of acute type I glaucoma. The bad cosmetic result and increased astigmatism have caused a search for a new operation to replace the "snip and tear" iridectomy.

Some surgeons perform a trephine operation, even in a red congested eye, and excellent results have been obtained. This is rather surprising, as one would expect the outpouring of serum and fibrin to close the trephine opening. I feel sure that the good results are due in many of these cases to the peripheral iridectomy. When the trephine opening drains satisfactorily, hypotony may be expected, as the base pressure is normal at the time of operation and a trephine has a large drainage-carrying capacity. Hence cataract formation is more likely to occur.

O'Brien recommends a peripheral basal iridectomy, and I have started performing this operation in these cases of type I primary glaucoma. In a recent communication Dr. Paul Chandler, of Boston, tells me that he has commenced performing this operation in cases of type I primary glaucoma and that he is pleased with his results to date, though his series of cases is still small. In the few cases in which I have used it, control is adequate so far.

Indications for Peripheral Iridectomy in Type I Primary Glaucoma.

Peripheral iridectomy can be expected to function adequately only in the absence of anterior peripheral synechiæ. This should be verified by gonioscopy. When this procedure is not possible it can be assumed that there are no anterior peripheral synechiæ in the following instances: (i) When there is a history of a first attack of not more than forty-eight hours' duration. (ii) When the base pressure is normal or nearly so. (iii) In unilateral type I primary glaucoma when the base pressure of the affected eye is not more than three to five millimetres of mercury (Schiötz) when compared with that of the normal eye.

Treatment of the Second Eye in Type I Glaucoma.

The second eye should be cared for as follows. Miotic therapy must be used until the eye under treatment is dealt with.

For cooperative patients, who can report for examination every six months or whenever any untoward event occurs to the eye, the use of miotics only is permissible. The patient should be warned that the drops do not cure the condition, but only control it, and that he must use them regularly, morning and night, and before entering a dark room for any length of time. He should be examined every six months, when a careful history about corneal œdema should be taken and a Schiotz reading, fields of vision test and gonioscopic examination carried out. Type I primary glaucoma is not masked as much as type II primary glaucoma, and in most cases the patient experiences corneal œdema or fifth nerve pain before any visual loss occurs. In these cases miotic therapy is reasonable if the patient is cooperative.

When the surgeon cannot rely on the patient's cooperation in the future for any reason, whether because of the state of his intelligence or because of his inaccessibility, what is to be done? Is it justifiable to discharge the patient from hospital and hope for the best? The safest procedure is to perform a peripheral iridectomy, which has practically no complications and gives a good cosmetic result, whilst ensuring immunity from an attack of glaucoma in the future.

The technique recommended is to perform a scratch incision two millimetres behind the limbus under a conjunctival flap. Dr. Chandler suggests doing it at the "10 o'clock" position, as this leaves the "12 o'clock" position available for any further surgical measures.

Type II Primary Glaucoma.

When possible, patients with type II primary glaucoma should be treated with miotics for as long as there is no field loss. An unreliable patient is in far greater danger of loss of vision in this type of primary glaucoma than a patient with type I primary glaucoma, because corneal œdema is the exception rather than the rule, and central vision is retained until an advanced stage of the disease. The same warnings should be given to the patient that the eye-drops will not cure the condition, and it should be stressed that treatment should never be abandoned.

The patient should be examined every three months, the tension, fields of vision and fundus examinations being carried out on each occasion.

Because of the insidious nature of the condition, any patient having miotic treatment for type II primary glaucoma who is overdue for his progress examination should receive a letter. In public hospital clinics the almoner should handle these patients.

When it is suspected that treatment will not be carried out faithfully, or when the patient cannot report every three months for examination, cyclodialysis should be advocated if the base pressure is normal or only slightly raised. More advanced stages require a trephine or Lagrange operation.

If the patient is unreliable the second eye should also be subjected to cyclodialysis if a positive result is obtained to the water-drinking test.

In the early stages of type II primary glaucoma, cyclodialysis controls the condition adequately and gives a good cosmetic result; further, it does not complicate future surgical measures.

SUMMARY.

1. There are two distinct types of primary glaucoma, the first type being caused by angle crowding and the second type by impeded absorption of aqueous in the region of Schlemm's canal.

2. The terms "narrow-angle" and "wide-angle", "congestive" and "non-congestive" and "chronic simple" are all open to criticism; "angle crowding" and "non-angle crowding" or simply "type I" and "type II" are suggested as better names.

3. A classification is given.

4. A discussion of both types of primary glaucoma is given and a peripheral iridectomy is recommended for early type I primary glaucoma and cyclodialysis for early type II primary glaucoma.

NOTE ON THE ESTIMATION OF PROTEIN BY THE BIURET METHOD WITH THE USE OF A PHOTOELECTRIC COLORIMETER.[1]

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THE Biuret method for the estimation of protein has been used extensively in clinical laboratories in the past few years. The original Kjeldahl method, which has always been the standard, requires more time and space than are readily available. The copper sulphate specific gravity method, which is widely used for urgent estimations because of the rapidity of determination, is limited in its application because its accuracy is impaired by changes in specific gravity of the blood other than those due to protein variation. Therefore it cannot be used for patients with a high blood urea or blood sugar content or for those who have recently had transfusions. The Biuret estimation provides a quick but reliable alternative method which can be conveniently adopted. The protein in a batch of six specimens of serum can be estimated in an hour, whereas the minimal time required to complete a small batch of macroscopic Kjeldahl estimations is four hours.

Many workers have noted difficulties in the preparation of a stable and convenient Biuret reagent. Kingsley (1942) made progress by using a "one-piece" reagent containing copper sulphate and sodium hydroxide in one solution, but it was not sufficiently stable for routine laboratory work. It consists of 500 millilitres of 14% sodium hydroxide solution and 100 millilitres of 1% copper sulphate solution.

Weichselbaum (1946) stabilized the reagent by the addition of sodium potassium tartrate and potassium iodide. His original solution has a high copper content and a low alkali concentration. He recommends a "dilute" reagent containing one-fifth the copper content for use with photoelectric instruments.

Gornall *et alii* (1949) confirmed Weichselbaum's findings and fully investigated the effect of different concentrations of the constituents. They proved that a minimal 3:1 ratio of tartrate to copper sulphate is necessary if the reagent containing moderate amounts of alkali is to remain stable for longer than a few weeks. The addition of potassium iodide to prevent "auto-reduction" is not essential if pure reagents are available.

These workers do not state for how long the reagent remains stable, but imply that it should keep indefinitely. This has not been found to be the case in this laboratory.

Experimental Investigation.

Variations in Calibration Curves with Different Batches of Reagent.

The purpose of this communication is to present the procedure adopted for satisfactory standardization of the reagent for routine work. At first the dilute Weichselbaum reagent containing 0·25% copper sulphate solution was tried. The calibration of a graph was a simple matter, a straight line being obtained when the galvanometer readings were plotted against the protein concentration, which had been estimated by duplicate Kjeldahl determinations. After two months it was found that the readings gave low results. The graph line appeared to have moved to the left, and in the normal range of serum protein values the figures obtained were as much as one gramme *per centum* too low. The Biuret reagent had developed a slight white deposit, and even after filtration a slight turbidity appeared when it was mixed with serum. The standardization of a freshly prepared reagent did not give a graph line identical with that obtained with the original solution.

Effect of Temperature on Calibration Curve.

Temperature also has an effect on the development and intensity of the Biuret colour. Wolfson (1948) and Gornall

[1] This work was made possible by a grant from the National Health and Medical Research Council.

et alii (1949) noted this in a series of experiments at different temperatures. The laboratory temperature had risen considerably in the two months' interval previously mentioned, so this factor was also concerned in the altered graph line. There was found to be a 2° increase in the galvanometer reading over the normal range for every 10° C. rise. This effect is reversible. Therefore 30° C. was chosen as a temperature convenient for the test at all seasons. The test tubes containing the protein solutions and the Biuret reagent are warmed to this temperature and maintained there by being placed in a beaker of water at 30° C. in an incubator for thirty minutes. Readings can be made at temperatures within 2° of 30° C. without any appreciable effect on the result.

Suitability of the Biuret Reagent.

The Weichselbaum reagent as modified by Gornall *et alii*, containing 0·15% copper sulphate solution, was finally chosen as the most satisfactory one for routine use with our "Evans E.E.L." colorimeter. It consists of 0·15% copper sulphate solution, 0·6% sodium potassium tartrate solution, 3·0% sodium hydroxide solution, and 0·1% potassium iodide solution. The specimens of serum are accurately diluted one in twenty. To two millilitres of diluted serum eight millilitres of the above-mentioned reagent are added.

It must be stressed that several points on the calibration graphs should be checked at frequent intervals if reliable assays are to be obtained. One batch of this modified solution was found to give accurate results for five months. The original solution tested was not reliable for two months. In a routine clinical department the reagent should be prepared only in sufficient quantity for the tests for three months, and checked at fortnightly intervals.

Good agreement with the Kjeldahl standard method has been found when several laboratory workers made the determinations. In a series of 18 specimens of serum the error averaged from + 2·4% to − 2·2%. This is much lower than the variations with the copper sulphate specific gravity method on blood samples from pregnant patients. Liddelow (1950) found errors up to two grammes *per centum*—a total error of 20%.

The Determination of Albumin-Globulin Ratios.

The Biuret method may be applied satisfactorily to albumin-globulin ratio determinations. The method of Gornall *et alii* (1949), who adapted the Howe procedure, was used. The sodium sulphate reagent was stored at incubator temperature to allow for the low temperature in most Melbourne laboratories in winter. To avoid temperature dilution errors in the estimation of the absolute amount of protein present, the pipetting of the serum and sodium sulphate solution was done at 22° C., the lowest temperature to which the sodium sulphate solution may be cooled without crystallization.

The mixture is then left in the incubator for half an hour. Addition of ether and thorough mixing just before centrifuging are necessary to obtain a clear separation of the globulin precipitate.

The albumin is estimated in the same way as the total protein content, the sodium sulphate present causing no alteration of the Biuret colour. The results can be read from the same calibration curve.

Summary.

It has been shown that the Biuret method as modified by Gornall *et alii* (1949) is a simple, reliable method for serum protein and albumin-globulin ratio determinations in a routine clinical laboratory.

It is important that regular checking of the calibration curve be made, as serious error may not otherwise be detected. The photoelectric colorimeter may be working normally, but the Biuret reagent is not always stable. The calibration curve must be restandardized with each batch of reagent, and this must be frequently rechecked if reliable results are to be assured.

The effect of temperature on the reaction is stressed.

Acknowledgements.

My thanks are due to Dr. Vera Krieger, who made some of the original estimations, and for help in the presentation of results, and to Miss B. Liddelow and Miss M. Browning for providing some of the Kjeldahl determination figures.

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USE OF A 12-VOLT ULTRA-VIOLET BULB FOR THE DIAGNOSIS OF RINGWORM INFECTIONS OF THE SCALP.

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APPARATUS for the fluoroscopic examination of ringworm of the scalp available in Australia consists of an ultra-violet lamp with an attached Wood's glass filter.

There is available in America the "Purple X" bulb (Dennie, 1947), which has the advantage of being small and easily manipulated. However, a report by O'Farrell (1948) indicates that the "Purple X" bulb does not cause

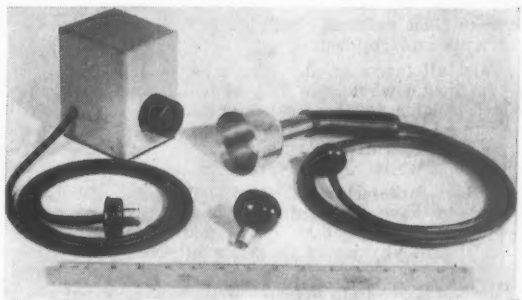

FIGURE I.

Twelve-volt fluorescent lamp, showing transformer, bulb and reflector on grip handle. (By courtesy of Audio-Visual Activities, Proprietary, Limited.)

fluorescence in cases of infection by the *Microsporon lanosum* (*Microsporon canis*). In Sydney, cultural studies have shown that by far the majority (over 90% in my own series) of cases of ringworm of the scalp are caused by *Microsporon lanosum*.

I have found that a useful substitute for the present apparatus available is a "Mazda" 12-volt special ultra-violet bulb. It is small and inexpensive. The power source is a transformer. Microsporon infections of the scalp examined by this bulb show the characteristic greenish fluorescence identical with that produced by ultra-violet light filtered through Wood's glass. In two cases of endothrix infection

dull whitish fluorescence as described by Lewis and Hopper was seen. One case of leptothrix has been investigated and fluorescence was exhibited. I have so far had no opportunity of investigating cases of infection by *Microsporon audouini*, of favus or of *Tinea versicolor*.

The advantages of this bulb over the ultra-violet lamp with an attached Wood's glass filter are as follows. (i) The bulb is easy to manipulate, being held in the hand, mounted in a suitable grip and reflector. (ii) The complete apparatus is in the vicinity of one-quarter of the cost of those at present available. (iii) In cases in which manual epilation of the child's scalp is indicated, the assembled lamp can be lent to the parent for home use.

The advantages over the "Purple X" bulb are as follows. (i) This bulb has caused fluorescence in all cases of *Microsporon lanosum* infection examined by me. (ii) The "Purple X" bulb has a relatively shorter life.

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ANGIOCARDIOGRAPHY.

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DURING a visit abroad in 1947 by one of the authors the rapidly expanding subject of congenital heart malformations, their investigation and their treatment, came under observation in various centres. The subject of this article, angiocardiography as a diagnostic measure, was observed in some detail.

Various techniques were witnessed, most of them somewhat crude, but it seemed that here was a graphic diagnostic method eminently suitable for diagnostic elucidation in infants and children.

Whilst all facets of any case must be joined to produce the diagnostic whole, the help of which angiocardiography seemed capable appeared considerable. It also appeared to have more than diagnostic importance; it gave to the surgeon pre-operative details of vascular arrangements and dimensions which were of great value.

Cardiac catheterization, also being extensively used, seemed to have great limitations in the pædiatric age group; small veins take only small catheters, and the difficulties of physics in catheters of small bore are quite considerable.

Therefore it did appear that, in addition to the immeasurably important clinical history and examination, angiocardiography was a method worthy of extensive trial.

This report is an attempt to show what has been achieved over the past two years at the Children's Hospital, Melbourne, with this fascinating procedure.

As far back as 1931 Forssmann attempted to demonstrate the cardiac chambers and great vessels by cardiac catheter and radioopaque material. In 1935 Laubry *et alii* produced a beautiful series of pictures by injection of opaque material into a cadaver heart. These interesting pictures illustrate fairly well the normal functional anatomy of the heart and great vessels, but of course it is a very different matter to produce equal clarity and definition in the rapidly acting heart of the living subject.

In 1938 Castellanos, Perieras and Garcia injected living infants' hearts at early ages, and since then there has been a spate of work on the subject all over the world, with constant attempts to improve definition, by increasing the rapidity of exposures so that important phases may not be missed, by the combining of oblique and antero-posterior views, and even by the use of X-ray cinematography.

After some trials and tribulations we have evolved a method by which it is possible to obtain a series of remarkably clear and often beautiful pictures of the chambers and great vessels of the heart, in both antero-posterior and left anterior oblique views.

Material and Scope.

In all, some 98 angiocardiograms have been prepared in 43 children. In the early stages four children with clinically normal hearts and of varying ages were selected, and angiocardiograms of these were used as normal controls (Figures I to IV). The rest of the series has consisted of patients with cyanotic and non-cyanotic congenital heart lesions, with two exceptions—one child was shown to have a rheumatic heart and the other a pulmonary arteriovenous aneurysm. The ages of the children varied from three months to fourteen years, most falling into the six to ten years group. A few of the cyanotic children were in poor physical condition, but the procedure was carried out in these cases with the special aim of helping to decide whether surgery could be of benefit.

Mortality.

In this series two deaths have followed the procedure of angiocardiography; both the subjects were cyanotic children. The first case occurred about one week after the films were taken, and the child's condition followed a downhill course of diarrhœa, increasing cyanosis and peripheral heart failure. In this case post-mortem examination revealed a most unusual lesion—the pulmonary veins were opening into the superior *vena cava*, there was no septal defect, and the only way blood could reach the left side of the heart and aorta was through an enormous patent *ductus arteriosus*. How far the angiocardiogram had precipitated this failure it was difficult to assess, but it was felt that for a boy to carry on with this lesion to the age of ten years was rather remarkable.

The second death occurred in a young girl about two hours after her angiocardiogram was prepared, when she collapsed suddenly as she was recovering from her anæsthesia. Previously she had caused no concern. Post-mortem examination confirmed the diagnosis of a pure pulmonary valvular stenosis.

Since anæsthesia for this procedure has been stopped there have been no further cases which have caused any concern at all.

Technique.

Films.

With the early cases a single large cassette was used, which could be moved through a tunnel, being exposed in sections. With this four films only could be obtained, and the time interval between exposures had to be varied to enable the dye to be followed through all the cardiac chambers.

More recently, a rapid cassette-changing tunnel has been used, the cassettes being moved manually but exposed automatically when in position. With this some nine or ten films can be obtained within five seconds. The exposure time is always kept to a bare minimum and is usually one-fiftieth of a second. The first film of a series is usually exposed one second after the commencement of the injection of dye.

The Contrast Medium.

A 70% diadone compound, "Vasiodone", has been used in this series, the material being carefully kept at blood heat before injection, to make sure that crystallization does not occur. Intravenous test-dosing with one millilitre of "Vasiodone" is always carried out, but no untoward reactions have occurred.

The "Vasiodone" is injected as rapidly as possible (usually in less than two seconds) in order to obtain the most satisfactory contrast X-ray pictures. Amounts vary

ILLUSTRATIONS TO THE ARTICLE BY MOSTYN L. POWELL AND HENRY G. HILLER.

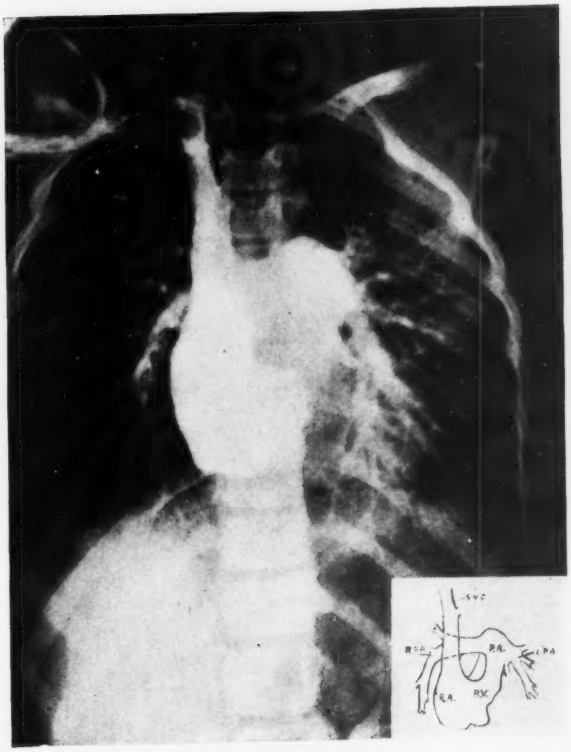


FIGURE I.

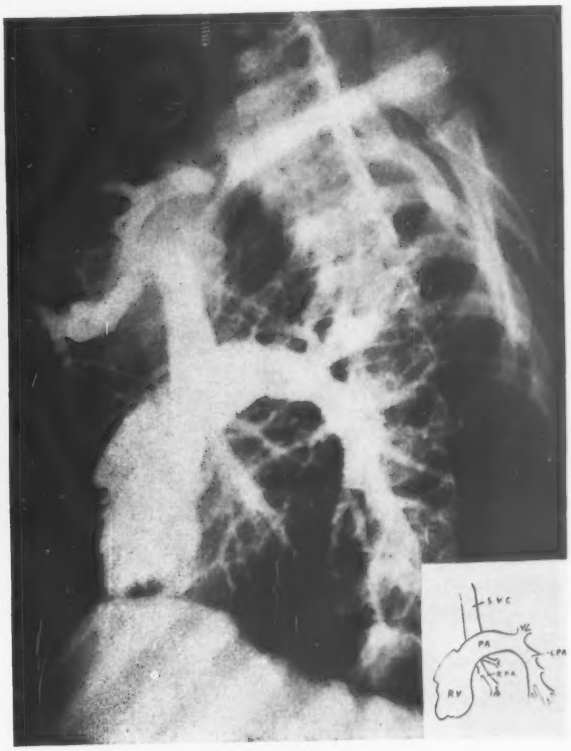


FIGURE II.

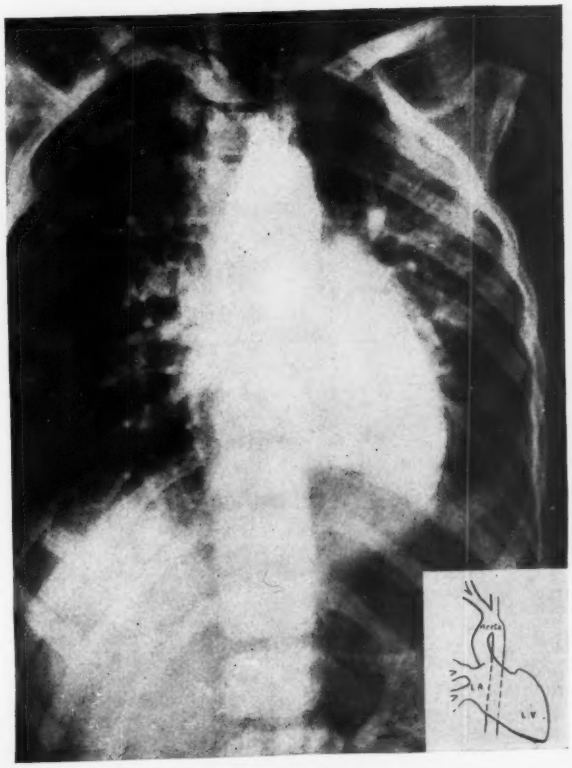


FIGURE III.

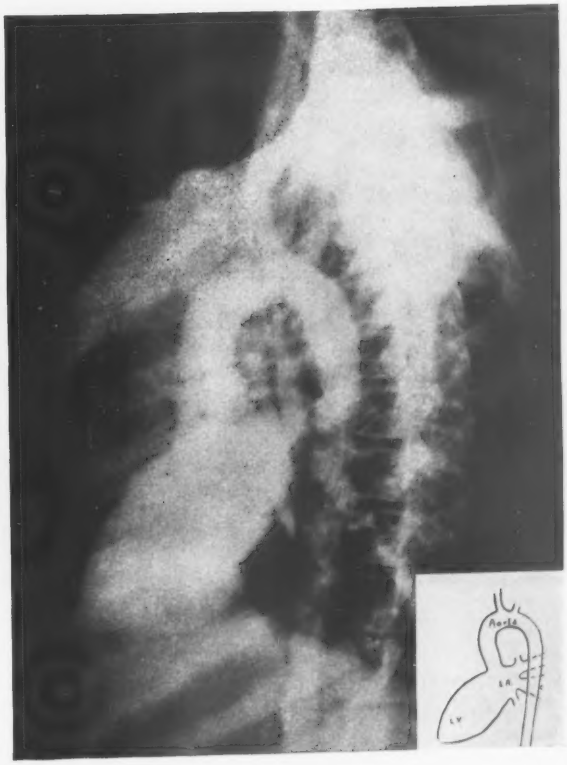
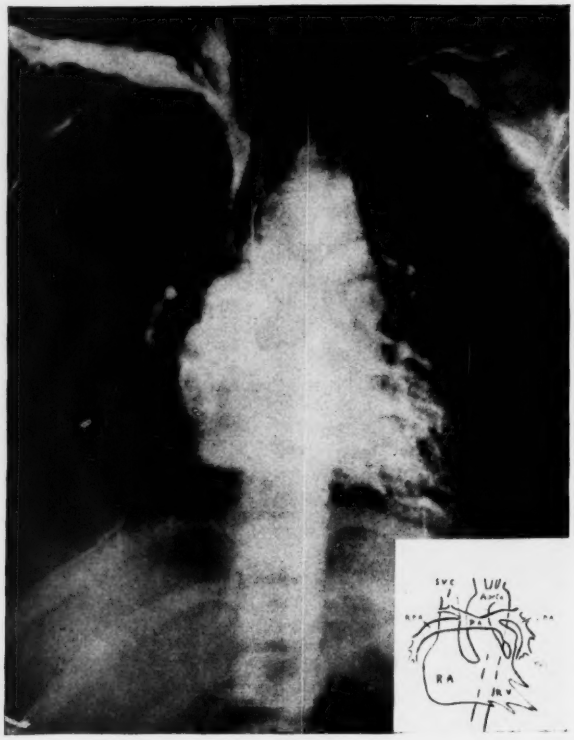


FIGURE IV.

ILLUSTRATIONS TO THE ARTICLE BY MOSTYN L. POWELL AND HENRY G. HILLER.



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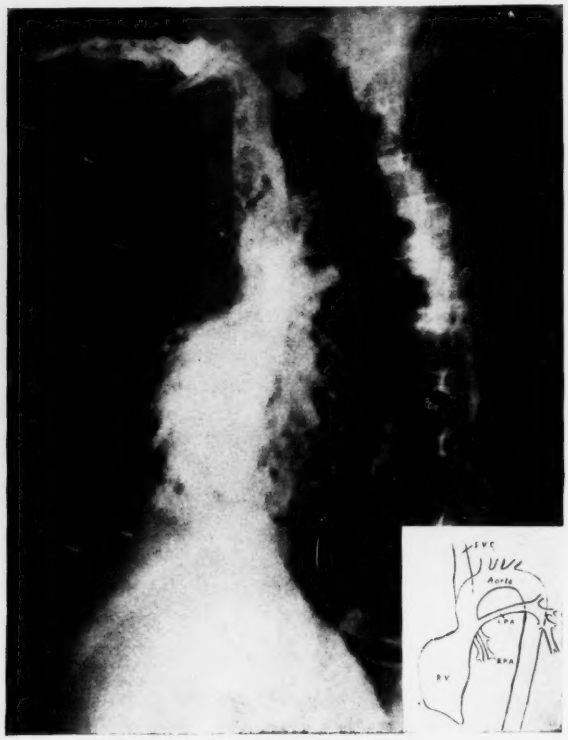

FIGURE VII.

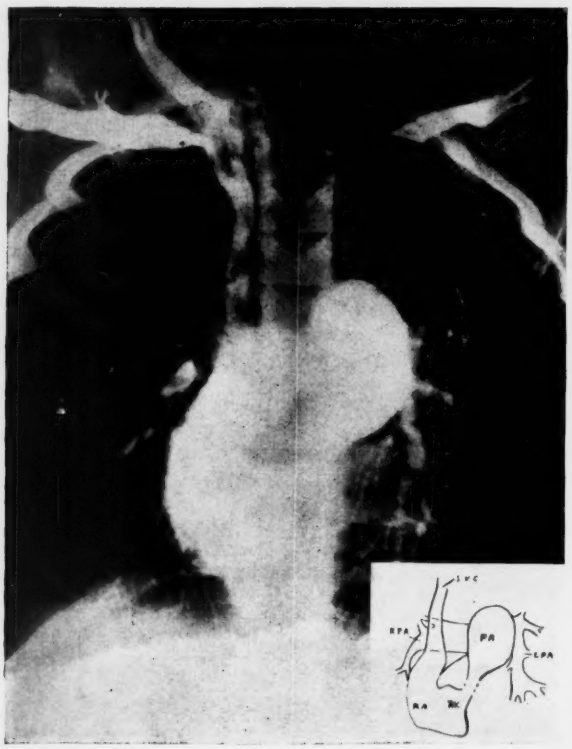

FIGURE VIII.

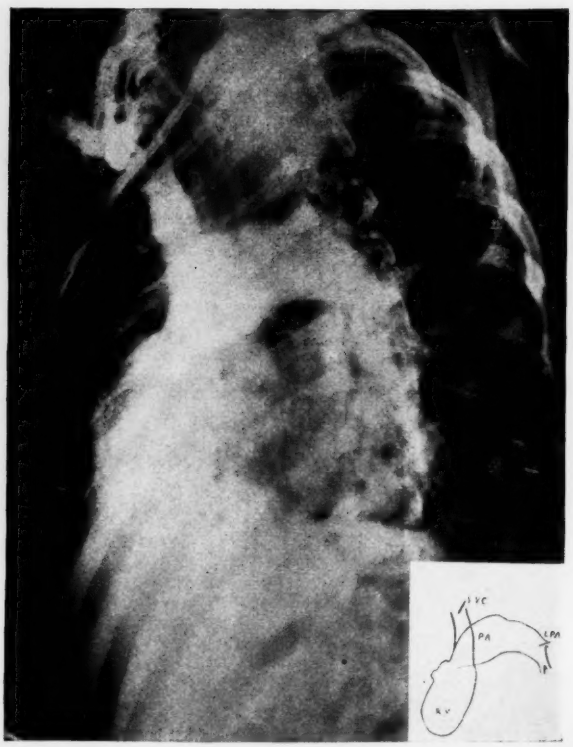

FIGURE IX.

ILLUSTRATIONS TO THE ARTICLE BY MOSTYN L. POWELL AND HENRY G. HILLER.

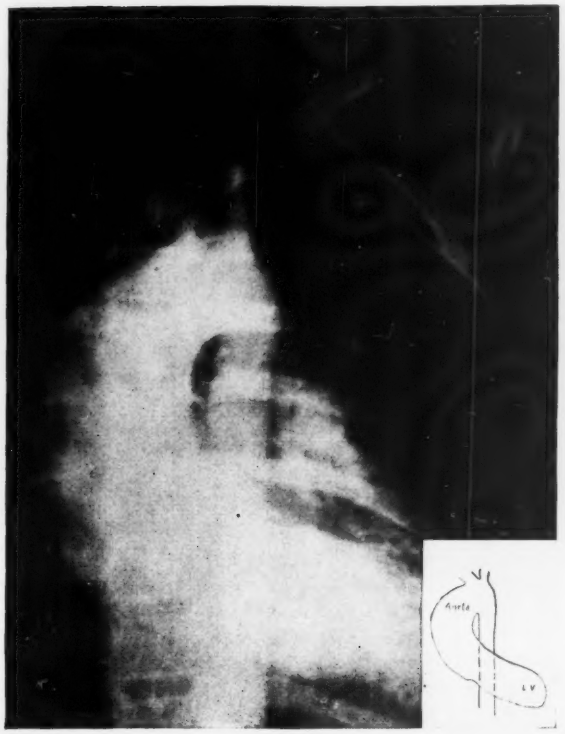

FIGURE X.

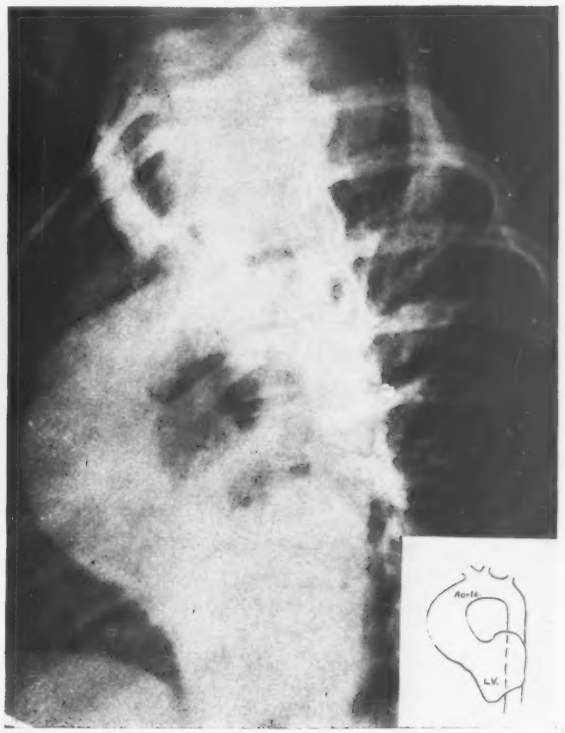

FIGURE XI.

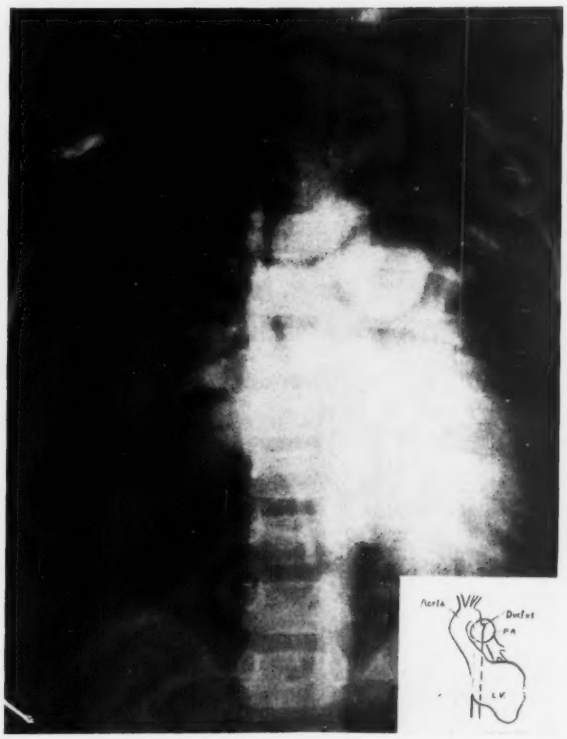

FIGURE XII.

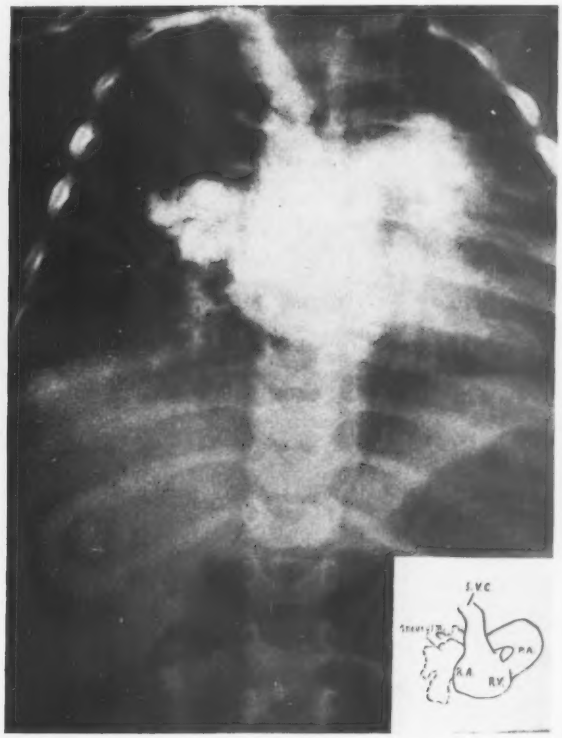

FIGURE XIII.

ILLUSTRATIONS TO THE ARTICLE BY JOHN A. McLEAN.

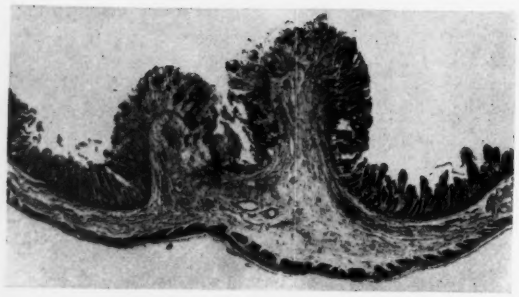

FIGURE II.

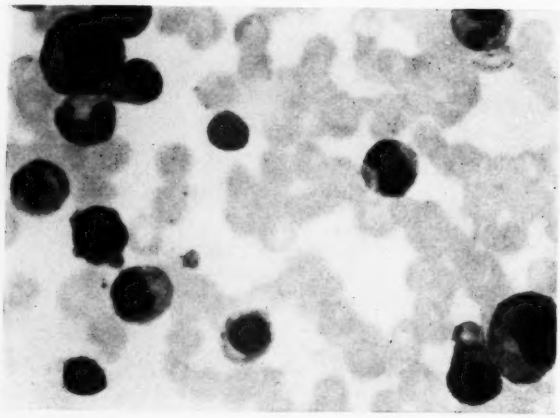

FIGURE IVB.

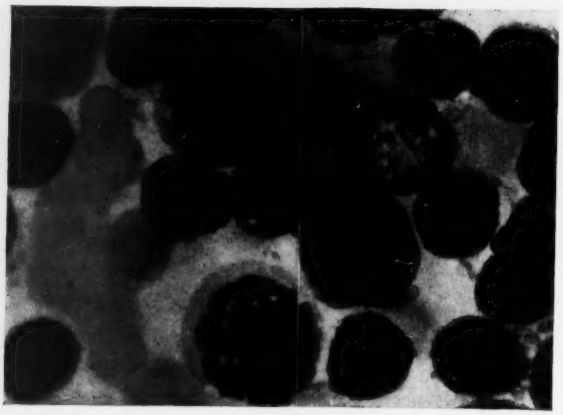

FIGURE IVA.

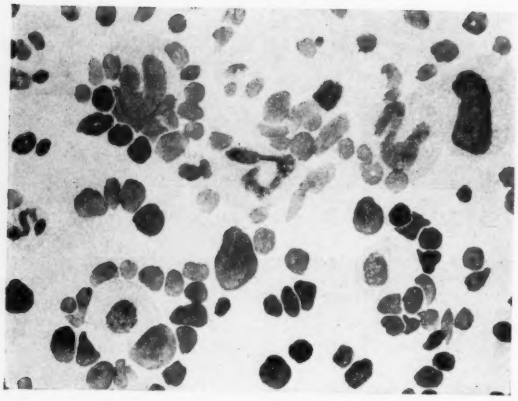

FIGURE V.

ILLUSTRATIONS TO THE ARTICLE BY E. G. McQUEEN.

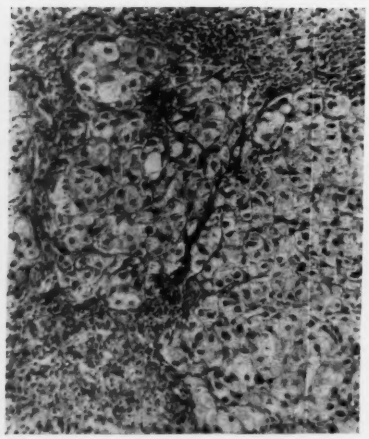

FIGURE I.

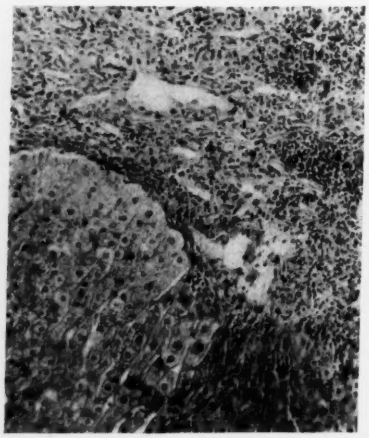

FIGURE II.

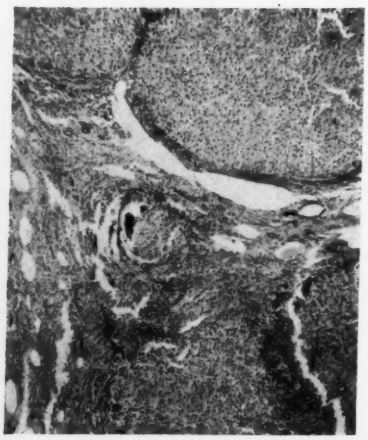

FIGURE III.

from 15 to 45 millilitres, depending on the size of the child under investigation, and on no occasion has any difficulty been experienced through rupture or tearing of the vein during the injection.

The "Vasiodone" produces a transitory and unpleasant sensation of heat, often accompanied by muscular and joint pains, nausea, and on occasions even vomiting. These effects wear off very rapidly. No anaphylactoid reactions have been noted.

A second injection of "Vasiodone" is usually given. This is never undertaken until half an hour after the completion of the first, to allow most of the "Vasiodone" from the first injection to be excreted by the kidneys.

FIGURE V.
Syringe and attachments.

Apparatus for Injection.

A special glass and metal syringe is used for the injections, with handles so that added leverage can be obtained. This is screwed into a "T" connexion and this in turn into a cannula (Figure V). This cannula is selected as being the largest which can be inserted into the chosen vein. In all cases the superficial veins at the elbow are used, and except where specially contraindicated, the right arm is used in preference to the left. By so doing it is found that there is less likelihood of obscuring the aorta and vessels in the neck. Also positioning of the patient is made easier.

The "T" connexion is used so that intravenous saline can be run through the cannula both before and between injections, its patency thus being ensured.

Position.

The prone position is used in all cases, and films are routinely taken with the patient in the antero-posterior and left anterior oblique positions. It is found better to use the latter position first, as a number of children find difficulty in holding the rather uncomfortable pose, especially if they have been on the X-ray table for some time. No attempt can be made to get most of the children to hold their breath, although a few of the older ones are very good in this respect.

Anæsthesia.

During the early work either mild sedation or intravenous injection of "Pentothal" was used. It was later decided that if anæsthesia was to be used, the presence of a skilled anæsthetist would be required, and a number of cyclopropane, gas and ether anæsthetic agents have been administered.

Contrary to what is usually stated, it has been found that cyclopropane is not an ideal anæsthetic agent for this procedure, as respiratory arrest and spasm appear on a few occasions. Therefore, towards the end of this series no anæsthesia has been used as all, it being found that although discomfort and an unpleasant sensation of heat are experienced, the children will cooperate sufficiently for a second series of films (if required) and appear to forget the whole procedure within a day or so.[1]

Circulation Time.

During some of the early work the circulation time was calculated before the angiocardiography was performed; this was done by the injection of fluorescein, the arm to tongue time then being estimated by means of an ultra-violet lamp. This procedure was not carried out for long, as it was found to be of little help in foretelling the rate of flow of the diadone compound. Apparently such a factor as the increased force and speed of the larger injection of diadone often makes its circulation through to the aorta much quicker than the calculated time would suggest was possible.

With the technique described, the pictures which are obtained give us a distinctly new impression of the functional anatomy of the heart. For example, it is apparent that the terms "right" and "left" as applied to auricles and ventricles are misnomers; it would be far more descriptive to say "the anterior or pulmonary auricle and ventricle, and the posterior or systemic auricle and ventricle". The "left" auricle is, almost mathematically, a mid-line and posterior structure. The site of the mitral valve is interesting: it is very posterior in position, which explains why its murmurs are so characteristically transmitted well back into the left axilla.

Interpretation of Films.

In the interpretation of films our two main methods of approach are direct and indirect.

Direct Method.

With the direct method obvious abnormalities of flow or definite variations in size or position of great vessels are noted, and lack of filling or over-filling of lung fields is observed.

A good example is seen in the tetralogy of Fallot, in which, owing to the overriding of the aorta, this vessel takes a large share of the incoming dye and fills much earlier than normal and simultaneously with the pulmonary artery, which is seen to be notably smaller than normal. This early filling of an overriding aorta is a direct observation of abnormality of extreme diagnostic importance. Similarly, the observation of notably small pulmonary arteries is a direct diagnostic feature. The combination of an early and simultaneously filling aorta with normal or large-sized pulmonary arteries is a fairly direct diagnostic indication of the Eisenmenger complex, which resembles the tetralogy except that there is no pulmonary stenosis.

[1] Since this article has been written, patients submitted for angiocardiography have been given mild "Seconal" sedation, and it has been found easier to control apprehension and to gain cooperation.

Another direct observation may be seen in the left anterior oblique view when an aorta obviously arises from the right ventricle, as in transposition of the great vessels.

Indirect Method.

With the indirect method, whilst it may not be possible to identify an abnormal vessel or chamber, the time of filling of a chamber or vessel may be distinctly observed and deductions drawn therefrom. For example, in a patent *ductus arteriosus* there may be opaque material entering the pulmonary artery long after it should have passed therefrom, indicating that a shunt is occurring. (We firmly believe, however, that the most important diagnostic weapon in the patent ductus is not the juvenile angiocardiograph but the matronly stethoscope.)

A good example of indirect diagnosis occurred recently and was not appreciated by us at the time. It occurred in a boy with an extraordinary condition of an anomalous venous return, whereby the whole of the oxygenated blood from the lungs in the pulmonary veins flowed into the superior *vena cava*, travelled from there through the right auricle and right ventricle, and went out through a huge pulmonary artery to the lungs. The systemic circulation was supplied by an enormous ductus leading from the pulmonary artery to the aorta. The left auricle was blind and a small left ventricle appeared to have little function. In this case, twenty-three seconds after the injection had stopped there was still opaque material in the superior *vena cava*, the right auricle and ventricle, for what, as we discovered at post-mortem examination, were obvious reasons.

A knowledge of the normal angiocardiographic anatomy and circulation times, combined with direct and indirect application of them, is the normal diagnostic technique.

Reports of Cases.

A number of interesting cases have been selected and brief case histories and angiocardiogram findings given. These cases have been chosen mainly because some lesson can be learnt from the evaluation of their angiocardiograms.

Case I.

J.S., a boy, aged ten years, had been cyanosed for some years. A basal systolic murmur and thrill were found, with clubbing of the fingers. Investigation revealed moderate polycythæmia, a right axis deviation in the electrocardiogram, and an X-ray picture showing a normal-sized heart with a concave left border and relatively translucent lung fields. The angiocardiogram confirmed the diagnosis of Fallot's tetralogy and showed simultaneous filling of aorta and stenotic pulmonary artery. The right and left pulmonary arteries were also visualized (Figures VI and VII).

Comment.—In a case such as this it is possible for the surgeon to approach the operation with a clearer mental picture of the exact relative positions and sizes of the arterial trunks which he hopes to anastomose. It is important if possible to visualize the size and position of the right and left pulmonary arteries as well as the parent trunk.

Case II.

G.P., a girl, aged twelve years, had been known to have a congenital heart lesion since she was eighteen months old. She had little impairment of exercise tolerance, and no cyanosis had been noted. A systolic murmur and thrill were to be found at the base of the heart; they were not conducted to the neck. No polycythæmia was present, and the electrocardiogram showed some right axis deviation. Straight X-ray pictures showed a prominent pulmonary artery segment with congestion of the lung fields. Otherwise the contour of the heart was considered normal. The angiocardiogram revealed a moderate degree of pulmonary stenosis with gross dilatation of the main pulmonary artery. There was poor filling of the lung fields. The diagnosis of congenital pulmonary stenosis was then suggested (Figures VIII and IX).

Comment.—The post-stenotic dilatation is interesting in a number of these cases and the mechanism of its production is not well understood. Angiocardiography should be of immense help in these cases when division of the stenotic area is being contemplated.

Case III.

J.B., a girl, aged nine and a half years, gave no history of disability. Her basal systolic thrill and murmur had been discovered at routine examination. The murmur was transmitted into the neck. The electrocardiogram and X-ray films were all normal. Angiocardiography showed an enormous dilatation of the ascending aorta, and with difficulty a stenotic area could be made out in the region of the aortic valves. The diagnosis of congenital aortic stenosis was thus confirmed (Figures X and XI).

Comment.—Again, the gross post-stenotic dilatation of the aorta should be noted. It has been found to be a far more obvious feature in subjects of aortic stenosis subjected to angiocardiography than the actual stenosis itself.

Case IV.

E.L., a girl, aged three and a half years, when first examined was considered possibly to have a patent *ductus arteriosus*, but the typical murmur could not be heard. The blood pressure was 110 millimetres of mercury, systolic, and 55 millimetres, diastolic, and the electrocardiogram was normal. X-ray plates and screening showed a large cardiac outline with normal lung fields. The angiocardiogram showed what appeared to be the ductus filling from the aorta and causing revisualization of the pulmonary trunk throughout the whole series of films. Since that time the characteristic murmur of a patent *ductus arteriosus* has appeared, and this child is at present awaiting operation (Figure XII).

Comment.—The angiocardiogram will only rarely depict the actual ductus. When the size of this vessel and the dilution of dye passing through it are remembered, this is not surprising. In this case the angiocardiogram was of diagnostic value and has since been confirmed by the appearance of the typical machinery murmur.

Case V.

K.M., a male baby, aged sixteen months, had a history of cyanosis for many months. With great difficulty a systolic murmur was picked up to the right of the sternum about the third and fourth right intercostal spaces. X-ray examination showed a shadow in the right lung, especially in the middle lobe. No definite conclusion was reached, but it was suggested that this was vascular in origin. The angiocardiogram confirmed the presence of an arteriovenous aneurysm of the right lung, especially of the middle lobe. Whilst awaiting operation, this baby suddenly collapsed and died. Post-mortem examination confirmed the diagnosis (Figure XIII).

Comment.—Although angiocardiography is largely restricted to the diagnosis of heart disease and especially of congenital heart disease, there are occasions when lesions of the lung itself can be diagnosed by its use. The above case is a good example of this. In another case an unsuspected segmental collapse was discovered only after angiocardiography had revealed it.

Conclusion.

What, then, is the future of this method of investigation? Merely to produce pictures, however beautiful, is not sufficient to justify a procedure which on occasions can cause anxious moments. We feel that the limits to the relief of cardiac abnormalities from surgery are not yet in sight and that the more accurate the diagnosis of these lesions, the more sure one can be in advice and prognosis.

As a major advance in diagnostic procedure angiocardiography must be granted a firm position, and particularly does this apply to the prepubertal age group.

Summary.

1. A description of the technique of angiocardiography as carried out at the Children's Hospital, Melbourne, is given.

2. The use of this as a diagnostic aid is discussed.

3. Some examples of cases and films are given.

Acknowledgements.

To Dr. Colin Macdonald and Dr. Colin Grant, of the X-ray department, we are indeed grateful for the helpful advice and complete freedom they have granted us in the

department. Dr. Margaret McClelland, anæsthetist to the hospital, has given us tremendous help upon the theoretical and practical aspects of anæsthesia in our cases. All members of the honorary staff have freely offered their patients to us, and to them we extend our gratitude. Mr. Murphy, the Children's Hospital photographer, has been most helpful in the production of the various X-ray plates and photographs. Upon Mr. Harold Anderson, who is in charge of the technical side of the X-ray department, fell the burden of designing the extraordinarily ingenious yet simple device with which our procedures were carried out; without his inventive skill and technical knowledge this work would not have been possible, and it is stimulating to realize that he is bent on achieving a still higher technical standard in the future.

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Legends to Illustrations.

FIGURE I.—Normal angiocardiogram: antero-posterior at 2·5 seconds.

FIGURE II.—Normal angiocardiogram: left anterior oblique at 2·5 seconds.

FIGURE III.—Normal angiocardiogram: antero-posterior at 5·0 seconds.

FIGURE IV.—Normal angiocardiogram: left anterior oblique at 5·0 seconds.

FIGURE VI.—Fallot's tetralogy: antero-posterior at 2·0 seconds.

FIGURE VII.—Fallot's tetralogy: left anterior oblique at 2·0 seconds.

FIGURE VIII.—Pulmonary stenosis: antero-posterior at 2·5 seconds.

FIGURE IX.—Pulmonary stenosis: left anterior oblique at 2·5 seconds.

FIGURE X.—Aortic stenosis: antero-posterior at 6·0 seconds.

FIGURE XI.—Aortic stenosis: left anterior oblique at 6·0 seconds.

FIGURE XII.—*Ductus arteriosus*: antero-posterior at 6·0 seconds.

FIGURE XIII.—Pulmonary arterio-venous aneurysm: antero-posterior at 2·5 seconds.

TREATMENT OF ACUTE LEUCHÆMIA BY FOLIC ACID ANTAGONISTS.

By JOHN A. MCLEAN,
Melbourne.

FOLIC ACID is a necessary factor for the growth of bacteria and it is also known to be a nutritional requirement of experimental animals and of man. The effect on cell growth of the folic acid conjugates and antagonists has been a subject for cancer research. In 1944 Leuchtenberger *et alii* reported that a folic acid concentrate, which was later shown to be pteroyl triglutamic acid, had an inhibition effect on the growth of sarcoma in mice. Subsequently Little *et alii* (1948) found that folic acid had a stimulating effect on the growth of Rous chick sarcoma, and that folic acid antagonists inhibited the growth of the tumour. Rhoades *et alii* (1949) also demonstrated an inhibitory effect of folic acid antagonists on the growth of sarcoma 180 in mice. In another neoplasm—namely, transplanted mammary tumours in mice—Higgins and Woods (1949), at the Mayo Clinic, found that an inhibitory effect was produced by aminopterin, and that this could be modified by the administration of folic acid.

This experimental work demonstrated the pronounced effect of these compounds on the growth of certain types of neoplasm; but when the drugs were given to patients suffering from cancer the response was not so dramatic as had been expected, and the lesion regressed in only a limited number of cases (Taylor *et alii*, 1948).

However, a striking improvement was found in cases of acute leuchæmia; Farber *et alii* (1948) found that an apparent accelerating action in acute leuchæmia was produced by folic acid conjugates, and this finding prompted him to use the biological antagonists of folic acid, which he discovered had an inhibitory effect on the growth of immature leuchæmic cells.

Of the various antagonists the most effective was found to be 4-amino'pteroylglutamic acid (aminopterin). This substance has a similar chemical structure to folic acid, from which it differs by the addition of an amino group in place of the hydroxyl group on the pteridine ring (Figure I). Other similar but less effective folic acid antagonists are a-methopterin, amino-an-fol and amino pteropterin.

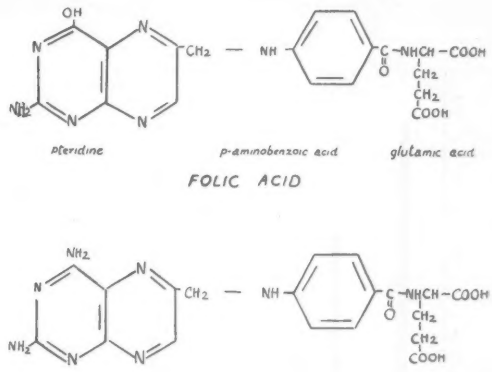

FIGURE I.
Chemical structure of folic acid and aminopterin.

These drugs have been the subject of clinical trial in many research centres in the United States of America, and the results which have been reported show that a remission can be produced in cases of acute leuchæmia. The remissions are characterized, not only by clinical improvement shown by the disappearance of symptoms and regression in size of lymph glands and spleen, but by a change towards normal findings in blood and bone marrow examinations. The leuchæmic cells, although they are greatly reduced in number, are temporarily checked only, and when the drug is discontinued the condition recurs.

If it were possible to continue the use of the folic acid antagonists in such a dose as to keep the leuchæmia controlled the prognosis of this disease would be changed; but owing to the toxic effects treatment cannot be prolonged indefinitely. These toxic effects are characterized by ulcerative stomatitis, anorexia, nausea and vomiting with diarrhœa, hæmorrhage, alopecia and loss of weight. Further, there is an effect on normal bone marrow cells, and a macrocytic type of anæmia develops.

Folic acid antagonists appear to be most effective in inhibiting the growth of immature cells. Berman *et alii* (1949) found that stem cells, granulocytes and immature lymphocytes decreased in number, but mature lymphocytes were relatively unaffected. Gunz (1950) found *in vitro* that aminopterin, when added to cultures of human leuchæmic cells, produced a considerable inhibition of mitosis.

In a study of normal dogs who had been given aminopterin, Thiersch and Phillips (1949) found a sprue-like

syndrome with diarrhœa, leucopenia and a depleted bone marrow in which there was an increased number of hypersegmented polymorphonuclear cells, giant metamyelocytes and megaloblasts. In a study of the bone marrow in man, Thiersch (1949) found after prolonged treatment with folic acid antagonists that megaloblasts appeared; but, in contrast to the picture in pernicious anæmia, the general cellularity was decreased.

The mode of action of these compounds is not known. It is possible that they substitute for folic acid and are accepted as such by the cell, but cannot be utilized, with the result that the cell dies.

Report on 22 Cases.

During the past two years I have treated 22 patients suffering from acute leuchæmia with folic acid antagonists. All these patients have been seriously ill with a predominating immature blast cell in the bone marrow. In many instances the types have been difficult to classify by cellular morphology, even with the aid of oxydase and supravital stains, and in such cases the immature cells have been described as blast cells. The following drugs and doses have been used: aminopterin, one milligramme; a-methopterin, five milligrammes; amino-an-fol, 50 milligrammes. The results of treatment are shown in Table I. A remission has been classified as complete when both the clinical condition improves and the blood and bone marrow examinations reveal approximately normal values. The incomplete remission is one in which the clinical condition has improved but the blood and bone marrow remain in a leuchæmic state. It will be noticed that the best results occurred in children, in half of whom complete remissions were obtained. In adolescents and adults there was no case of complete remission, but partial remissions occurred in approximately half the cases. Although the leuchæmia was inhibited to a greater or less extent in 50% of the patients treated, death ultimately occurred in all cases.

The varying response to treatment in different individuals did not depend on the dose of drug administered, as in some cases a remission occurred after a small dose, whereas in other cases a similar effect was not manifest until a much larger dose had been given over a prolonged period of several months.

There were toxic manifestations in all patients and in some instances death was directly due to these effects. The most serious toxic symptoms were anorexia, vomiting, diarrhœa and hæmorrhage. Post-mortem examinations in two cases revealed extensive ulceration in the jejunum, and examination of histological sections revealed necrotic changes and ulceration in the mucous membrane (Figure II). In the surviving epithelium immediately adjacent to the zones of necrosis was found irregular glandular formation with large bizarre nuclei and mitotic figures rather suggestive of malignant change. Autopsy also revealed numerous small focal necroses in the liver, lung and spleen glands. It was not certain whether these were a direct effect of the drug, or whether they were due to terminal septicæmia as indicated by masses of bacteria which were found in these areas.

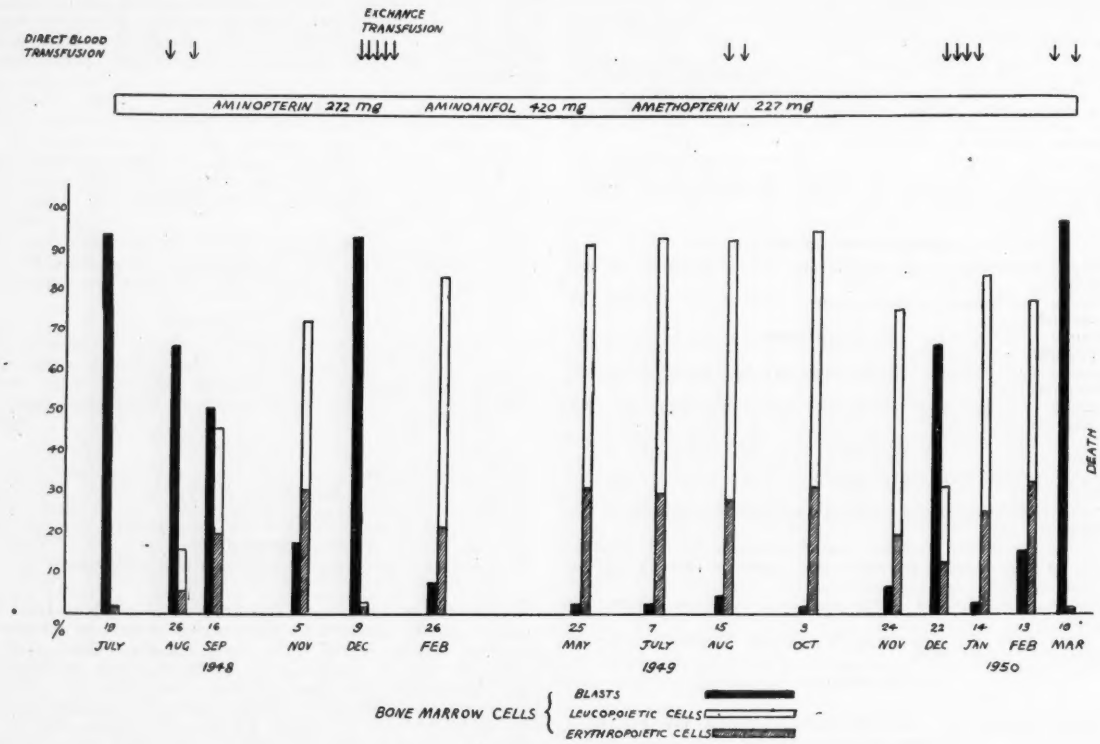

FIGURE III.
Graph of bone marrow differential counts in case of J.T.

Throughout the period of treatment bone marrow aspirations were regularly performed. In several of the acute cases the condition was aleuchæmic, and marrow aspiration was essential in diagnosis and as a guide to treatment. In all cases in which the effect of the drug was studied, most information was obtained from serial bone marrow films. Figure III shows a graph of the bone marrow counts in a patient (J.T.), who was treated over a period of one year and eight months. This boy, aged eight years, had a complete remission which lasted for nine months, during which time bone marrow findings were within normal limits. The remission occurred after an exchange transfusion which, according to Bessis (1949), can have such an effect in a certain number of cases of acute leuchæmia. However, in another case (patient S.R.)

TABLE I.

Results in a Series of 22 Cases of Acute Leuchæmia. The Final Result in all Cases was Death.

Subject.	Age. (Years.)	Sex.	Duration of Treatment.	Total Amount of Drug in Milligrammes.			Type of Remission.[1]
				Aminopterin.	Amino-an-fol.	a-Methopterin.	
E.S.	3	F.	23 weeks.	18	—	—	Complete (3 months).
J.T.	8	M.	1 year 8 months.	272	420	227	Complete (9 months).
M.S.	2·5	F.	23 weeks.	34	—	—	Complete (1 month).
R.R.	12	M.	4 months.	25	—	—	Partial.
N.O'D.	9	M.	1 year 1 month.	97½	600	550	Complete (3 months).
D.P.	11	M.	13 weeks.	27	—	—	Incomplete.
S.R.	6	M.	10 weeks.	33	—	—	Partial.
L.O'D.	15	F.	6 months.	227	481	—	Partial.
R.B.	15	M.	4 months.	86	—	—	Partial.
H.T.	35	M.	12 months.	200	—	—	Partial.
M.D.	49	F.	3 months.	60	—	—	Partial.
R.D.	56	F.	7 months.	146	—	—	Partial.
L.M.	49	F.	6 weeks.	—	—	170	No remission.
D.A.	42	F.	4 weeks.	16	—	—	No remission.
J.C.	23	M.	6 months.	150	220	—	Partial.
E.D.	19	F.	3 weeks.	18	—	—	No remission.
E.H.	29	F.	17 days.	23	—	—	No remission.
A.D.	17	M.	6 months.	148	—	—	Partial.
R.McN.	20	M.	17 days.	21	—	—	No remission.
W.N.	10	F.	11 months.	6	—	483	Complete.
B.B.	4	M.	6 months.	10	—	366	Partial.
R.H.	3·5	M.	4 months.	263	—	—	Partial.

[1] A remission is classified as complete when the clinical condition is improved and the bone marrow counts are normal, and incomplete when the clinical condition only is improved.

in which an exchange transfusion was given, there was an apparent accelerating effect on the leuchæmia, which was subsequently inhibited by aminopterin.

The effect of treatment on the leuchæmic cells of the bone marrow is seen in Figure IV, which shows a reduction in blast cells and revival of normal marrow cells. In this case before treatment the blasts and lymphocytes numbered 98% of the total cell count, and in a search of 200 low-power fields no megakaryocytes were seen. After treatment the bone marrow film appeared normal and there were six megakaryocytes in 200 low-power fields.

Toxic effects of the drug on the bone marrow after prolonged treatment were shown by the presence of megaloblasts and giant metamyelocytes in films (Figure V).

In all cases antibiotics were given for infection, which was occasionally an associated cause of death. Hæmorrhage, which was also a serious complication, was successfully treated by the direct transfusion of unmodified blood.

From the results in the series of cases herein reported, it is concluded that remarkable remissions in acute leuchæmia can occur with the use of folic acid antagonists, but treatment is necessarily restricted by the toxic effect of the compounds on normal tissues.

Summary.

In experimental cancer in animals folic acid antagonists produced regressions of cell growth, and in man inhibition of acute leuchæmia has been found. In a report of 22 cases of acute leuchæmia, remissions occurred in half the cases. Better results were obtained in children than in adults. Serious toxic effects occur and may cause death.

Acknowledgements.

Acknowledgement is made to Dr. Sidney Farber, who made the drugs available and has given helpful advice in their use. Thanks are also due to Dr. R. W. Linton, of the Lederle Laboratories Division, American Cyanamid Company, for a generous supply of folic acid antagonists. The photomicrographs were made by Mr. Matthaie, of the faculty workshops, University of Melbourne.

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Addendum.

Growth factors recently isolated in the United States of America known as citrovorum factor and folinic acid have been shown, in experimental animals, to prevent toxic effects of folic acid antagonists.

Schoenbach *et alii*, in *The Journal of the American Medical Association* of December 30, 1950, at page 1558, have reported cases in which ulceration in the mouth due to aminopterin was healed by administration of citrovorum factor.

It is hoped that these substances will prevent the toxicity of aminopterin on normal tissues without also diminishing the effect on abnormal leuchæmic cells.

Legends to Illustrations.

FIGURE II.—Jejunum from S.R., showing necrosis and ulceration of mucous membrane.

FIGURE IVA.—Bone marrow films from N.O'D., showing blasts predominating before treatment.

FIGURE IVB.—Bone marrow films from N.O'D., showing normal myeloid cells after treatment.

FIGURE V.—Bone marrow film from W.N., showing macrocytes, megaloblasts and giant metamyelocytes, after six months' treatment with a-methopterin.

Reports of Cases.

CIRRHOSIS OF THE LIVER IN EX-PRISONERS OF WAR (JAPAN): A PRELIMINARY COMMUNICATION.

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HEPATOMEGALY in ex-prisoners of war (Japan) is a not uncommon finding. It is frequently associated with dyspepsia and general malaise, and when there is tenderness of the enlarged liver, together with episodes of fever, and particularly when there is looseness of the bowels or frank diarrhœa, the condition is usually regarded as amœbic hepatitis and treated as such.

Although at times great improvement may occur, frequently the response is disappointing, suggesting that amœbic infection is not the sole pathological lesion. In the four cases reported in this paper cirrhosis of the liver was suggested by the clinical and biochemical findings and confirmed by biopsy.

Case I.

A truck driver, aged thirty years, had been a prisoner of war in Malaya. During captivity he is recorded as having suffered from malaria, beriberi, ulcers of the legs, gastro-enteritis, amœbiasis and dermatitis. He had malaria on several occasions following his relapse. He was in the habit of drinking three or four glasses of beer per day and of smoking two or three ounces of tobacco per week.

He was admitted to hospital on October 12, 1950, with the complaint of soreness in the epigastrium for months, coming on two hours after meals, and unrelieved by food or alkalis. He complained also of vague general malaise but no nausea. He was passing two or three motions each day, of (he considered) normal consistency. He had noticed himself at times to be feverish at night.

On examination of the patient, the liver was enlarged three to four fingers' breadth below the right costal margin. The spleen was palpably enlarged. There were a considerable number of capillary angiomata over face, arms and chest.

On October 16, 1950, estimation of serum proteins showed a total of 8·1 grammes *per centum*. Of this, albumin comprised 3·9 grammes *per centum* and globulin 4·2 grammes *per centum*.

On October 20 the result of a cephalin cholesterol flocculation test was positive ("+++" in twenty-four hours).

On October 31 the Van den Bergh reaction was direct positive, the serum bilirubin content was 0·6 milligramme *per centum*, and there was a great increase in urinary urobilinogen.

On November 10 the patient's serum prothrombin value was 90% of normal, the serum alkaline phosphatase value was 22 King-Armstrong units, and the thymol turbidity test showed a value of eight units. Findings from a gastric test meal produced a normal curve.

On November 28 the patient's erythrocytes numbered 4,520,000 per cubic millimetre, and the hæmoglobin value was 13·0 grammes *per centum*. There were 8300 leucocytes per cubic millimetre, of which 28% were neutrophile cells, 37% lymphocytes, 3% monocytes and 32% eosinophile cells.

On January 9, 1951, the erythrocytes numbered 4,780,000 per cubic millimetre, and the hæmoglobin value was 14·2 grammes *per centum*. The leucocytes numbered 8300 per cubic millimetre, of which 41% were neutrophile cells, 38% lymphocytes, 2% monocytes and 19% eosinophile cells.

Radiological examination of the chest, including fluoroscopy, revealed no abnormality. With Graham's test the gall-bladder was not visualized. No calculus was seen. X-ray examination after barium meal and barium enema revealed no abnormality, and with barium bolus revealed no evidence of œsophageal varices.

On November 30, 1950, and on several subsequent occasions after antiamœbic treatment, vegetative forms of *Entamœba histolytica* were found in the stools.

The results of Wassermann and Kline tests were negative.

On November 14, 1950, liver (needle) biopsy (E.G.M.) was performed. The histological appearances were reported on as follows: "Diffuse overgrowth of new connective tissue in portal tracts, which is active and progressive, with much fibroblastic proliferation." (See Figure I.)

On January 2, 1951, because of a slight rise in temperature, exacerbation of upper abdominal pain and tenderness of a portion of the swollen liver margin, exploratory needling was performed. No pus was found.

A course of emetine treatment made no significant difference to his condition. He was kept at rest in bed and given a diet of high protein and low fat content with methionine supplement.

Case II.

The patient was an agricultural scientist. He too had been a prisoner of war in Malaya, and during captivity had suffered from malaria, beriberi (with affection of the heart in 1943 and 1945) and amblyopia. He was treated in hospital in December, 1945, and January, 1946, for symptoms considered then to be due to malaria. Hepatomegaly was recorded at that time. He was in hospital again in 1948 with a diagnosis of amœbic hepatitis. At that time also the diagnosis was made of "anxiety state". He was in the habit of drinking two or three glasses of beer per day. He was readmitted to hospital on December 13, 1950, when he complained of recurrent attacks of diarrhœa, weakness and depression, and of loss of appetite.

On examination of the patient the liver was enlarged three fingers' breadth below the right costal margin. The spleen was palpable.

On December 20, 1950, the total serum protein content was 7·1 grammes *per centum*, of which the albumin content was 3·2 grammes *per centum* and the globulin content 3·9 grammes *per centum*. The serum prothrombin value was 100% of normal, and the thymol turbidity test yielded a value of three units. On December 22 the result of a cephalin cholesterol test was positive ("++++" in twenty-four hours).

Between December 13 and December 22 examination of nine stools revealed no amœbæ or cysts.

On December 19 X-ray examination after barium enema was carried out and the result reported as normal.

On December 22 sigmoidoscopy revealed no ulceration of the bowel, but a little blood-stained mucus was seen coming down from higher in the bowel.

On January 2, 1951, liver (needle) biopsy was performed (E.G.M.). The specimen obtained was reported on as follows: "Marked chronic inflammation and fibrous overgrowth in portal tracts." (See Figure II.)

A course of emetine treatment followed by "Yatren" enemata was given. With this, rest in bed and a diet of high protein and low fat content with methionine supplement his symptoms subsided and the liver seemed to become smaller.

Case III.

The patient was a timber worker, aged thirty-three years. During captivity in Malaya he had suffered from malaria, beriberi, dysentery and ankylostomiasis. He had been admitted to hospital on June 10, 1950, complaining of pain in the upper part of the abdomen during the previous two years. The liver was then found to be enlarged three fingers' breadth below the right costal margin and slightly tender. The spleen was reported to be just palpable.

Investigations at that time revealed the presence of hookworm ova in the stools. The results of tests for occult blood were also positive. No amœbæ or cysts were found on several examinations. Blood count, X-ray examination after barium meal, and chest X-ray examination revealed no abnormality.

On June 17 he was given a "hookworm bomb" consisting of tetrachlorethylene, three millilitres, with oil of cheno-

podium, one millilitre, followed by magnesium sulphate, half an ounce. He was discharged from hospital two days later.

He was readmitted to hospital on August 14, 1950, when his presenting complaint was of yellowness of the skin for five or six weeks. He stated that at the beginning of July, 1950, he had noticed lassitude, headache and pains in the limbs. A few days later he had had pain in the right hypochondrium, his urine had become dark in colour and his stools "creamy". His skin had then become yellow and itchy, and he had suffered from nausea. The yellowness of the skin persisted, but at the time of admission he did not complain of nausea, although his appetite was poor. He did not complain of diarrhœa.

On examination he was seen to be jaundiced, the liver was enlarged four fingers' breadth below the right costal margin, and the spleen was palpable. There were capillary angiomata over the arms, face and chest, and there was pronounced palmar hyperæmia. On specific questioning he said he thought that some of the spider nævi had been present for the last two years.

On August 17 the serum bilirubin content was 13·0 milligrammes *per centum*, the thymol turbidity test yielded a value of 30 units, the urinary urobilinogen content was much increased. The serum alkaline phosphatase content was 28 King-Armstrong units. The red-cell fragility was normal.

On October 21 the serum proteins amounted to 7·6 grammes *per centum*, of which 3·4 grammes *per centum* were albumin and 4·2 grammes *per centum* were globulin.

On October 24 the prothrombin value was 80% of normal.

Examination of stools on three occasions did not reveal amœbæ or cysts.

On October 24 liver (needle) biopsy was performed (E.G.M.). The specimen obtained was rather unsatisfactory, but served to show the presence of fibrotic change and some inflammatory cell infiltration.

The patient was treated by rest in bed and a diet of high protein and low fat content with methionine supplement, and improved considerably, his jaundice gradually disappearing.

Case IV.

A man, aged forty-four years, a farmer, had suffered during captivity in Malaya from malaria, dysentery, pellagra and hookworm. He stated that he consumed alcohol in moderation and smoked four ounces of tobacco per week.

He was admitted to hospital on May 15, 1950, when his presenting symptoms were soreness and swelling in the upper part of the abdomen for a period of twelve months. These were aggravated by lifting weights, by riding on his tractor, and by taking food. For twelve months he had noticed no blood or mucus in his motions. The patient stated that he had been subject to frequent bouts of malaise accompanied by joint pains. These he had attributed to malaria. During the last few attacks there had appeared a rash along the waistline, fading as the attack subsided.

On examination of the patient, the liver was enlarged two fingers' breadth below the right costal margin. There was an urticarial rash around the trunk at the waist. Apart from an apical systolic murmur there were no other significant clinical findings.

On May 29, 1950, the result of a cephalin cholesterol flocculation test was positive ("++" in twenty-four hours).

On June 2 the serum protein content was 7·0 grammes *per centum*, of which albumin amounted to 3·9 grammes *per centum* and globulin 3·1 grammes *per centum*.

Microscopic examination of the fæces revealed the presence of hookworm ova, but there were no amœbæ or cysts.

The results of blood counts were within normal limits, and the result of an agglutination test for brucella was negative.

The findings from X-ray examination after barium meal and barium enema were negative.

On August 14, 1950, at the request of another physician, laparotomy was performed for biopsy of the liver. The findings at operation were as follows: "Markedly enlarged, nodular, firm liver, somewhat greyish in appearance. Cirrhotic changes are widespread. No ascites present, no other pathology noted in abdomen." A small wedge was taken from the lower edge of the liver. The histological report on this specimen, a portion of which is shown in Figure III, was as follows: "The liver cells and liver lobules look perfectly healthy, but the capsule is greatly thickened and fibrosed, and shows a cirrhotic change with proliferation of small bile ducts and some round-cell infiltration. The portal canals contain some round-cell inflammatory infiltration also."

Discussion.

In Case III only was there a history of jaundice, and in this case there was evidence of liver damage before the hookworm treatment that precipitated it. In no case was there a history of excessive consumption of alcohol.

The experimental production of cirrhosis by dietary deficiency alone is now well known (Györgi and Goldblatt, 1939, 1942; Himsworth and Glynn, 1944; Abell *et alii*, 1950).

Work in a number of tropical and subtropical countries has shown the frequency of liver disease amongst the native populations (Fernando *et alii*, 1948; Trowell and Muwazo, 1945; Gillman and Gillman, 1945; Waterlow, 1947) and there seems little doubt that, although parasitic infections play some part, nutritional deficiency is the major ætiological factor.

The suggestion is offered that the cases of hepatic cirrhosis reported herewith are a sequel of nutritional deficiency during captivity. Case IV is particularly interesting in that although superficially the liver appeared to be grossly cirrhotic, section revealed the deeper areas to be essentially normal, a finding supported by the relative normality of hepatic function. This would suggest a lesion of the nature of that termed by Abell *et alii* "submassive necrosis", individual episodes of which were shown in their rats to be recoverable.

The object of this preliminary communication is to draw attention to cirrhosis as a cause of symptoms and of hepatomegaly in ex-prisoners of war. It is considered also that the potential dangers of anthelminthics in these subjects should be emphasized.

Acknowledgements.

I wish to thank the Chairman of the Repatriation Commission, the Principal Medical Officer of Queensland, and the Medical Superintendent of the Repatriation General Hospital, Greenslopes, for permission to publish these cases; also Dr. W. G. Harvey for his assistance in the preparation of this preliminary communication, and particularly for having directed my attention to Case IV.

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Reviews.

RECENT ADVANCES IN CHEMOTHERAPY.

To deal adequately with the extensive literature being published on chemotherapy, G. M. Findlay has found it necessary to rearrange his book; the third edition will appear in four volumes instead of one. Volume I[1] covers the chemotherapy of scabies and helminthic and protozoal diseases with the exception of malaria; the second volume will be devoted wholly to malaria; the third will deal with the chemotherapy of bacterial, rickettsial and virus infections; while the fourth will contain a survey of sulphonamides and antibiotics, with a discussion of the general principles of chemotherapy. More than two thousand reputable medical journals have to be scrutinized to keep pace with the published findings of workers in this subject; moreover, there is as yet no "chair" of chemotherapy in existence. Two factors hinder the work of the writer on chemotherapy: firstly, the absence of a wholly satisfactory classification of bacteria, which leads to confusion; and secondly, the multiplicity of names given by manufacturers to one and the same compound. The World Health Organization of the United Nations has made a start in an effort to standardize these matters.

Chemotherapy is a subject of great historical interest, and the author divides its development into three phases: first, pure empiricism; next, the period 1910 to 1935 during which protozoal, spirochætal and helminthic infections only were amenable to chemotherapy; and thirdly, the modern period associated with the chemotherapeutic control of bacterial infections by sulphonamides and antibiotics. The work is very comprehensive and includes a great deal of information on the pathology and treatment of animals both captive and domestic; for instance, one can find advice as to the treatment of elephants and sea-lions. It is interesting to note that David Livingstone, in 1858, published a paper on the use of arsenic in the treatment of horses suffering from "tsetse bite". The "blood brain barrier" in trypanosomiasis is discussed, and attention is drawn to findings as to the actual effects of drugs on the trypanosomes while they are in the organs of the tsetse flies themselves, and the various means of entrance of the parasites. A section sets out the essentials in the assessment of treatment of trypanosomiasis, namely, clinical symptoms, the protein content of the cerebro-spinal fluid, the cell count of the cerebro-spinal fluid, and the blood sedimentation rate.

The volume is divided into chapters which deal with the history of chemotherapy, chemotherapy of diseases due to insects, of helminthic infections, amœbiasis, babesiasis and other protozoal infections, leishmaniasis and trypanosomiasis, and concludes with a comprehensive list of authors and an index of subjects. It is well set up and printed; moreover, detailed lists of references are placed at the end of each section within the chapters, the countless numbered footnotes which such a work would require being thus avoided. The book is most comprehensive and should prove invaluable to medical schools, veterinary science schools, and agricultural colleges and all serious students of the subject as a work of reference.

HEART AND CIRCULATION.

AUSTRALIAN GRADUATES, who have visited London since World War II in search of further training in internal medicine, will agree that one of their most stimulating experiences has been clinical instruction from Dr. Paul Wood, now Director of the Institute of Cardiology at the National Heart Hospital, whose text-book "Diseases of the Heart and Circulation" has recently been published.[2] This work is a revelation of the qualities responsible for Dr. Wood's high reputation as a clinical teacher. He has condensed into a book, only half the size of similar texts, almost all modern cardiological concept and practice. This capacity for succinctness gives the reader little opportunity for relaxation, and at times leads the author himself into a frank but stimulating dogmatism.

The book begins with a chapter entitled "Approach to Cardiology", an attractive title which, however, covers merely the routine of clinical examination, and a sketchy description of laboratory yardsticks. We would prefer to see, exchanged for the first, the last chapter and one of the best, which deals with the differentiation of organic heart disease from Da Costa's syndrome, a perennial problem even for the experienced practitioner. Descriptions of radiological and electrocardiographic abnormalities follow, and these are better reread after the later systematic descriptions of the various ætiological types of heart disease have been covered. The electrocardiograms are especially well reproduced and arranged around an outline of Einthoven's triangle, while the teleradiograms vary in their clarity. Certain sections of the work stand out prominently as some of the best we have read. They are chiefly those which Dr. Wood has studied in the laboratory and ward, and which he has published elswhere, notably the chapters dealing with congenital heart disease, rheumatic carditis, the diagnosis of ischæmic heart damage, and hyperkinetic circulatory states. In the description of heart failure, the views of McMichael and his school are advanced, and one wishes that longer discussion could be devoted to this viewpoint, which Dr. Wood assisted to establish. Stead and Schroeder's work on the role of the kidney in œdema, in fact, information concerning the chemical and biochemical implications of cardiac failure, receives scant mention in comparison with that found in most American publications. Statistics are kept to a refreshing minimum. Dr. Wood accepts Prinzimetal's views as to the mechanism of the auricular arrhythmias; he is still not convinced that anticoagulants have proven themselves of routine value in the management of cardiac infarction. His description of the venous pulse is better than we have seen before, while the chapter on pulmonary heart disease alone is an outstanding monograph. Descriptions of the ætiology of hypertension, phæochromocytoma, and heart disease in pregnancy are relatively incomplete.

As in most first editions of this magnitude, there are scattered errors in type and spelling, and some of the radiographs have reproduced badly. An important and comprehensive bibliography follows each chapter. The book terminates in a magnificent forty-page index, which itself gives a lesson in differential diagnosis. As a concise yet thorough review of modern cardiology, or as an introduction and guide to intensive reading of any type in this field, this book is unsurpassed, and will achieve a world-wide reputation.

[1] "Recent Advances in Chemotherapy", by G. M. Findlay, C.B.E., Sc.D., M.D., F.R.C.P.; Third Edition, Volume I; 1950. London: J. and A. Churchill, Limited. 8″ × 5½″, pp. 636. Price: 36s.

[2] "Diseases of the Heart and Circulation", by Paul Wood, O.B.E., M.D. (Melbourne), F.R.C.P. (London); 1950. London: Eyre and Spottiswoode, Limited. 10″ × 6″, pp. 628, with many illustrations. Price: 70s.

Notes on Books, Current Journals and New Appliances.

ARCHIVES OF THE MIDDLESEX HOSPITAL.

Archives of the Middlesex Hospital, which was formerly published from 1903 to 1916, has now reappeared in a new series, of which Volume I, Number 1, is dated January, 1951. It is to be published quarterly. In an introduction to the first number of the new series Victor Bonney, who was associated editorially with the previous issues, surveys the journal's fourteen years between 1903 and 1916 and points to some of the notable papers published in that time, as evidence that then the Middlesex Hospital "made gifts to the general stock of professional knowledge of which it may well be proud". He points out that the reappearance of the *Archives*, as an outlet for the immense amount of clinical and scientific research which every year is carried on in the wards and laboratories of the hospital, has long been overdue. With the great development that has occurred in the hospital, he is confident that the new series will certainly equal and probably excel the old series. The first number contains articles on "Chronic Mastitis—a Non-existent Disease", arteriography of the abdominal aorta in vascular disorders, atypical abdominal tuberculosis simulating myeloid leuchæmia, toxoplasmosis, disorders of the cervical intervertebral disks, and reconstruction of the *vas deferens* after operation for sterilization. The printing and general production are excellent, and the journal should be able to stand comparison with any of its class. The publishers are E. and S. Livingstone, Limited, of Edinburgh. The annual subscription is £2 2s. and the price of single numbers 12s. 6d.

The Medical Journal of Australia

SATURDAY, JULY 28, 1951.

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MATERNAL MORTALITY IN THE UNITED STATES.

THE reduction by the United States of its 1949 maternal mortality rate to a figure less than 1·0 per 1000 live births is a matter for congratulation and must be very gratifying to public health authorities and to the medical profession generally in that country. This reduction is all the more striking when it is pointed out that the figure has declined steadily, with a drop every year, from 6·2 per 1000 live births in 1933. The 1949 figure has been calculated by F. G. Dickinson and E. L. Welker,[1] of the Bureau of Medical and Economic Research of the American Medical Association. A little confusion exists over the exact figure, because during 1949 a change-over took place between the fifth and sixth revisions of the International List of Causes of Death, but only 23 of the 49 States in the United States reported the maternal deaths for the year on the basis of both the fifth and sixth revisions. As the figure necessarily varies according to the revision used, Dickinson and Welker found it impossible to arrive at a "true" national rate. However, no matter what the basis, the rate is certainly less than 1·0 per 1000 live births. This is the first time in history, it is pointed out, that a large nation has brought its mortality rate to such a low level, and the measure of the achievement is brought home when it is realized that the risk of dying in childbirth in the United States is now approximately one-seventh of what it was a generation ago. The lowest rate for any nation yet published is said to be that of 0·9 per 1000 live births attained in Denmark in 1948. Dickinson and Welker quote as the latest available published rate for Australia the 1947 figure of 1·9 per 1000 live births. Other rates quoted (all per 1000 live births) are as follows: Canada, 1948, 1·5; England and Wales, 1947, 1·2; Finland, 1947, 2·1; Netherlands, 1947, 1·4; New Zealand (excluding Maoris), 1947, 1·1; Norway, 1947, 1·5; South Africa (rate per 1000 total births for Europeans only), 1947, 1·4; Sweden, 1945, 1·3; Switzerland, 1947, 1·8. Viewed beside the others, the Australian figure does not appear particularly creditable, but it is probable that the figure has decreased since 1947. Figures for New South Wales made available by the courtesy of W. J. Willcocks, of the Bureau of Census and Economics, Sydney, show a drop in the number of maternal deaths per 1000 live births from 1·87 in 1947 to 1·37 in 1948, and again 1·37 in 1949. In his recent R. H. Fetherston Memorial Lecture, Robert Fowler quoted the remarkable 1949 figure for Victoria of 0·77 maternal deaths per 1000 live births. It is certainly to be hoped that the Australian figure is being reduced to a rate of which we need not be ashamed. There is no valid excuse for it to be otherwise, as we have not, for example, the problems met with in the United States resulting from their large mixed population. It is worthy of note that some of the most creditable of the results obtained in the United States have been achieved by States in which problems of this type are great. Dickinson and Welker point out that it is entirely possible that the records made by some of these States still having higher maternal mortality rates may represent an accomplishment in social progress even greater than that recorded by States reporting the lower maternal mortality rates. "Nevertheless", they continue, "we can see that local authorities, well able to analyse the situation in their own community, are presented with a tremendous opportunity for community service in those States where maternal mortality still maintains a relatively important position in the health picture." This is, of course, a generalization with an application far wider than just in the United States. All States in Australia have not matched the Victorian figure of 0·77 per 1000 live births, and it is salutary to us to note that of the nine main divisions of the United States, four had a rate of only 0·7 per 1000 live births, and for only three were the figures above 1·0 per 1000 live births, these being 1·3, 1·4 and 1·8 respectively.

[1] *The Journal of the American Medical Association*, December 16, 1950.

SOLITUDE AND SILENCE.

IN every-day language we speak of a man in a state of solitude and also of him in a state of isolation. This generally means that the man is alone, but as a rule there is a subtle difference between the terms. Man may have solitude thrust upon him and he may also seek and enjoy it. On the other hand, to speak of a man in isolation generally implies that he has been put in a place apart from other men or that he finds himself alone, when he would rather follow or indulge his gregarious instincts. The incarcerated prisoner is in a somewhat different condition from that of the patient isolated because of his infection by one of the exanthemata. The one has been separated from his fellows because of something that he himself has done and the other because, as it appears to him, some fell disease has chosen to attack him. The one will be allowed to take his place in society again when those who removed him from it consider that he has expiated his fault; the other when processes going on inside his body have healed him or made him whole and given him entitlement to freedom. But it is solitude of a different kind which we would discuss. The subject is well stated in Bacon's essay "On Friendship" as follows:

> It hath beene hard for him that spake it to have put more Truth and untruth together, in few Words, then in that Speech, *whosoever is delighted in solitude is either a wilde Beast or a God.* For it is most true, that a Naturall

and Secret Hatred and Aversation towards Society, in any Man, hath somewhat of the Savage Beast; But it is most Untrue that it should have any Character at all of the Divine Nature; Except it proceed, not out of a Pleasure in Solitude, but out of a Love and desire to sequester a Man's selfe for a Higher Conversation; . . . But little doe Men perceive what Solitude is, and how farre it extendeth. For a Crowd is not Company; And Faces are but a Gallery of Pictures; And Talke but a *Tinckling Cymball*, where there is no Love.

Recalling that it has been said that solitude vivifies, but isolation kills, we may consider why men seek solitude, what they may hope to gain by it and also what mental and spiritual equipment those likely to achieve gain, should have. Here no doubt there will come to mind those who choose to live their lives in the seclusion of a religious order. Though possibly some of these persons are temperamentally unfitted to live cheek by jowl with those in the "madding crowd", most of them choose the cloistered life for reasons that can be understood only in the light of religious conviction and devotion to the Deity. That this life, sincerely lived, can give peace to the one who lives it and equip him with power for the battle of life in his own sphere and in the sphere of others who come to him for help, cannot be denied. And it is this that gives us a clue to what solitude can do for us. Solitude has been called the audience chamber of God and Blackie has written that:

> Converse with men makes sharp the glittering wit,
> But God to man doth speak in solitude.

Every man whose conscience is not dead, may pass through his own particular Gethsemane, but, relying on the right aid, he will emerge refreshed and with new vigour. But this sounds as though it had to do only with the great moments, the crises, of life, and was not of every-day concern. Emerson wrote: "Go cherish your soul; expel companions; set your habits to a life of solitude; then will the faculties rise fair and full within." He also wrote that he was sure that by going much alone a man would get more of a noble courage in thought and word than from all the wisdom that was in books. We may conclude then that to "go alone" for the ordinary man should be something like the occasional "retreat" enjoyed by certain religious bodies, an opportunity to take stock and to seek inspiration. Not everyone is fitted for this kind of venture; certain reserves of thought and experience are necessary. Abraham Cowley, who lived in the seventeenth century, wrote:

> The truth of the matter is, that neither he who is a Fop in the world is a fit man to be alone; nor he who has set his heart much upon the world; though he have never so much understanding; so that Solitude can be well fitted and set right, but upon a very few persons. They must have enough knowledge of the World to see the vanity of it, and enough Virtue to despise all Vanity; if the Mind be possest with any Lust or Passion, a man had better be in a Fair, than in a Wood alone.

The ability to benefit from solitude, like most other abilities of its kind, can surely be acquired.

Samuel Johnson thought that solitude might be dangerous to reason, without being favourable to virtue. While we grant that this is possible, we must be careful to distinguish from those who seek solitude, the man who is solitary because of what he is and does. The great leaders of men are solitary in this sense; they are also no doubt lonely, for they cannot always be self-sufficient. Aldous Huxley has said that the more powerful and original a mind, the more it will incline to the religion of solitude; and Ibsen in one of his plays writes that the strongest man in the world is he who stands most alone. In regard to dictators and such like, one is inclined to recall Bacon's reference to the "Savage Beast".

Bacon also observes that men do not perceive how far solitude extends. Of a truth a crowd is not company, for solitude is within a man; he need not be alone on a desert plain or on a mountain peak. Bacon quotes the "Latine Adage" as appropriate: "*Magna Civitas, Magna Solitudo.*" This leads to the subject of silence. The *magna civitas*, the big city, will be full of noise, clanging and discordant, but this will not necessarily disturb the solitude that is within a man. A human voice directed at him may disturb his thoughts and shatter his dreams and leave him in a state of complete confusion. The man of whom Yeats wrote that he would

> . . . arise and go now, and go to Innisfree,
> And a small cabin build there, of clay and wattles made;
> . . . . . .
> And live alone in the bee-loud glade,

would not notice the humming of the bees, but would resent the untimely intrusion of a human voice. He would, like most reasonable people, be sympathetic to Rupert Brooke, and even approve the violence of his language:

> And I knew
> That this was the hour of knowing,
> And the night and the woods and you
> Were one together, and I should find
> Soon in the silence the hidden key
> Of all that had hurt and puzzled me—
> Why you were you, and the night was kind,
> And the woods were part of the heart of me.
>
> And there I waited breathlessly,
> Alone; and slowly the holy three,
> The three that I loved, together grew
> One, in the hour of knowing,
> Night, and the woods, and you—
>
> And suddenly
> There was an uproar in my woods,
> The noise of a fool in mock distress,
> Crashing and laughing and blindly going,
> Of ignorant feet and a swishing dress,
> And a Voice profaning the solitudes.
>
> The spell was broken, the key denied me,
> And at length your flat clear voice beside me
> Mouthed cheerful clear flat platitudes.
>
> You came and quacked beside me in the wood.
> You said, 'The view from here is very good!'
> You said, 'It's nice to be alone a bit!'
> And, 'How the days are drawing out!' you said.
> You said, 'The sunset's pretty, isn't it?'
> . . . . . .
> By God! I wish—I wish that you were dead!

We remember that the Preacher wrote in the book "Ecclesiastes" that there was to every thing a season and a time to every purpose under the sun. Among one of the "times" which he named was: "a time to keep silence, and a time to speak". Those experienced in friendship know that two kindred souls may spend an evening of pleasure and satisfaction, say by the fireside, in contemplation with scarcely a word said. The gift of silence when the "time" for it has come is a golden gift, and he or she who possesses it is to be prized and honoured.

The end of the matter is that we shall do well to seek solitude now and again when we wish to commune with ourselves and to reorientate our ideas. We need not wander away alone to do this, but should be able to rely

on those near and dear to us to respect our moods. If we should feel the need to "sequester" ourselves this should be possible. Of course it goes without saying that when those about us have similar ideas, we should be as helpful as we expect them to be.

Current Comment.

RECTUM AND COLON SENSIBILITY IN RELATION TO ANAL CONTINENCE.

THE mechanism and significance of sensation in the rectum and colon are from the practical point of view very important, especially to the surgeon undertaking radical measures in the vicinity. This fact tends to receive emphasis when surgeons discuss "sphincter-saving" operations, in excision of the lower part of the bowel, and the difficulties encountered in any effort to retain for the patient satisfactory anal function. Unhappily rectum and colon sensibility with its relationship to the anal mechanism has not been understood as well as could have been wished, and the report of an investigation by two workers from Saint Mark's Hospital for Diseases of the Rectum and Colon, J. C. Goligher and E. S. R. Hughes,[1] should be welcomed for the light it sheds on the subject. These two investigators record observations on the sensations produced by balloon distension of the rectum and distal part of the colon in 40 normal subjects and in patients who had undergone various operative procedures involving interruption of the nerve supply to the bowel or removal of portions of the rectum. In the second group an attempt was made to correlate the findings with the functional result obtained. The distension was effected with a balloon mounted on the end of a narrow graduated rubber tube, which was inserted into the rectum and the lower part of the sigmoid colon through a sigmoidoscope; the instrument was then withdrawn over the tube, and the tube was connected to a pair of bellows and a mercury manometer. Distension of the bowel up to about 15 centimetres from the anal orifice (occasionally only 10 centimetres or as much as 25 centimetres) caused a sensation of fullness in the rectum, giving the patient a desire to pass wind or fæces—the "rectal" type of sensation. Distension above this level produced a purely abdominal sensation, referred to the suprapubic or left iliac region, and simulating a "wind" pain or intestinal colic—the "colonic" type of sensation. Interruption of the nerve supply to the rectum and colon by anæsthetic block or operative division showed that the colonic type of sensation is mediated by the sympathetic and the rectal type by the parasympathetic system. Goligher and Hughes point out that the two types of sensation accord with Hurst's findings in 1911, but the additional fact emerges that the distribution of the two types of sensation in the bowel does not always coincide accurately with the anatomical division into rectum and colon. They have also found that the rectum is more sensitive and discriminating than the colon: sensation can be elicited at a lower pressure in the rectum than in the colon, and the rectum can distinguish between flatus and fæces, a feat beyond the colon's powers. In these matters the experimental findings and circumstances of normal function are found to correspond.

Goligher and Hughes's findings bearing on anal function are particularly interesting. They found that balloon distension causing rectal sensation evoked a contraction of the external *sphincter ani* which appeared to be partly reflex and partly voluntary. This was never produced by colonic distension. It is pointed out that a rectal type of sensation never develops in the part of the colon leading to an abdominal colostomy opening, but that it may develop in an imperfect way in stumps of colon drawn down into the pelvis to restore continuity after sphincter-saving resections of the rectum. This appears to be related to the new anatomical position. Goligher and Hughes suggest that pressure on surrounding parts is a factor in the production of rectal sensation in normal subjects, but that it cannot be the only factor since the rectal sensation elicited in these colon stumps is much less delicate and discriminating than normal rectal sensation and requires a higher pressure to elicit it; it also seems to be of little value to the patient as a substitute for the sensory function of the normal rectum in the maintenance of anal continence. The view of Goligher and Hughes is that anal continence depends on the action of the external anal sphincter and the pubo-rectales, which are voluntary muscles capable of vigorous active contraction; they can see no role in this function for the internal sphincter. They advance reasons for regarding the exercise of anal continence as an essentially conscious activity—the initial contraction of the sphincter apparatus in response to a rise of intrarectal tension is entirely reflex, but voluntary contraction follows as the rectal sensation reaches consciousness, and subsequent actions (differentiation between fæces and flatus, and decisions regarding maintenance or relaxation of sphincter contraction) are entirely conscious processes. The point is stressed that anal incontinence may follow not only injury to the motor mechanism (for example, division of the anal musculature), but also damage to the sensory apparatus even though the muscles may be intact and capable of strong voluntary contraction. In sphincter-saving excisions of the rectum, scrupulous preservation of the external sphincter muscle, the *levatores ani* and the motor nerves may be followed by a poor functional result. This is because the rectum, with its essential sensory nerve endings, has been largely or entirely sacrificed; consequently, the patient receives inadequate warning of a sudden accumulation of fæces or flatus and so cannot contract his sphincters in time. Goligher and Hughes contend that the quality of the functional result in a sphincter-saving operation depends on the amount of ano-rectum preserved; with an ano-rectal stump of not less than eight to ten centimetres, measured from the anal orifice, function was found to be invariably good; with a stump of six to seven centimetres function was usually good, but sometimes was defective especially for flatus or liquid fæces. Thus they recommend that if a good functional result is to be ensured, the surgeon must preserve undamaged not only the sphincter muscles, but also at least six centimetres, and preferably eight centimetres or more, of ano-rectal stump with its parasympathetic nerve supply. The other problem associated with sphincter-saving excision of the rectum for malignant disease is that of local recurrence. This was well brought out by V. M. Coppleson, in a paper read to the New South Wales Branch of the British Medical Association in October, 1949, and by a number of experienced surgeons in the discussion that followed (see THE MEDICAL JOURNAL OF AUSTRALIA, March 18, 1950, pages 353 and 382). It offers serious objections to the whole principle of sphincter-saving operations; but it is nevertheless another story and should not be allowed to obscure the value of Goligher and Hughes's contribution to the problems associated with the maintenance of anal function.

[1] *The Lancet*, March 10, 1951.

ADRENALINE-CONTAINING CREAM AND RHEUMATISM.

MASSAGE with a cream containing adrenaline has been claimed to relieve pain from chronic fibrositis and other "rheumatic" conditions. Practitioners interested should read a report by E. G. L. Bywaters (published as a letter)[1] on a therapeutic trial designed at the request of the research subcommittee of the Empire Rheumatism Council. The effects of massage with, respectively, a proprietary product of this type and a control cream (similar but not containing adrenaline) were compared. It is concluded that "the effects . . . are for practical purposes the same".

[1] *British Medical Journal*, July 14, 1951, page 120.

Abstracts from Medical Literature.

PÆDIATRICS.

Lead Poisoning in Infancy.

NORMAN S. CLARK (*Archives of Disease in Childhood*, September, 1950) describes a case of lead poisoning in a four-months-old infant, resulting from contamination of drinking water by lead pipes in the house. The infant was breast fed until two weeks before the onset of its illness, but had drunk about a cup of water daily in addition to its feeds. The onset was with listlessness and vomiting for two weeks, followed by convulsions and facial paralysis. The cerebro-spinal fluid contained 80 milligrammes of protein *per centum*. The blood count showed hypochromic anæmia, but no punctate basophilia. Radiographs of the long bones showed characteristic dense bands at the ends of the metaphyses. Recovery occurred.

Circulatory Diseases of the Kidney.

WOLF W. ZUELZER *et alii* (*American Journal of Diseases of Children*, January, 1951) present a detailed clinical and pathological survey of certain major vascular injuries to the renal parenchyma that occur in infants with sufficient frequency to warrant attention. They state that, apart from congenital anomalies, pyelonephritis and tumours, renal disease is rare in infancy; but between 1940 and 1950 they have found 40 cases of severe vascular damage in 2058 autopsies performed on infants and children. Symmetrical cortical necrosis occurred in 11 cases. The necrosis was ischæmic, with patches resembling small infarcts in the least severe and a bandlike zone of necrosis extending throughout the entire cortex in the most severe. Tubules and glomeruli show varying stages of necrosis, and the blood vessels degeneration of their walls or thrombosis. The authors suggest that necrosis results from vasospasm or dilatation and stasis in the small renal arteries. The patients varied in age from one day to seven months. The precipitating illnesses were diarrhœa and dehydration, post-operative shock, erythroblastosis, septicæmia, shock following a difficult birth and cyanotic heart disease. The renal disease was often not expected. Œdema was present in one case, oliguria or anuria was recorded in five. The urine was examined in only six cases, three of the patients having albuminuria and two of these hæmaturia as well. Acute glomerular thrombosis occurred in two cases, both in infants with severe extra-renal infections. The authors state that the process seems to depend on the presence of organisms in the glomerular tufts, and is as a rule clinically cut short by the overwhelming effects of the systemic infection. If the patient survives the initial phase of such infection, the glomerular obstruction leads to hæmaturia, anuria and azotæmia. Since such infections can now be handled more adequately, the renal complication of glomerular thrombosis may become of greater clinical importance than heretofore. Arteriolar necrosis (acute malignant hypertension), previously not reported in infants, occurred in two cases; one patient was an eight-year-old boy and one an infant, who had lesions of *periarteritis nodosa* in some extra-renal vessels. Embolic occlusion of the renal artery occurred in four cases, the subjects being newborn infants. Two had diarrhœa, one dermatitis and one symptoms of cerebral hæmorrhage, due probably to cerebral embolism from the same source as that affecting the kidney. The authors state that this condition is not as rare as the recorded number of cases seems to indicate. Dehydration, embolism from the *ductus arteriosus*, or retrograde thrombosis from the umbilicus may be the cause. The clinical picture is characterized by abnormal urinary findings, a tendency toward anuria and azotæmia, and sometimes signs of embolism in other parts of the body. Ischæmic atrophy of the kidneys due to a gradual occlusion of the intrinsic renal arteries occurred in one case, the subject being a boy aged eight years. Thrombosis of renal veins, usually the result of diarrhœa and dehydration, occurred in 12 cases; the subjects were infants. The diagnosis is suggested by a sudden enlargement of one or both kidneys, hæmaturia and albuminuria and azotæmia. Diffuse hæmorrhagic infarction of the kidney without vascular thrombosis was found twice; in both cases the subjects were babies with severe infections. A lower nephron nephrosis, with necrosis of the distal convoluted tubules and loops of Henle, but with intact glomeruli and proximal convoluted tubules, occurred in four cases. The clinical picture of this disease is the passage of blood, blood pigment, albumin and casts, oliguria or anuria, azotæmia, hypertension with a mortality of 90%.

Galactosæmia.

GEORGE N. DONNELL AND STANLEY H. LANN (*Pediatrics*, April, 1951) report two cases of galactosæmia, a rare inborn error of metabolism that presents in the neonatal period with failure to thrive, hepatomegaly, slight jaundice, albuminuria and melituria, and a tendency to the development of lamellar cataracts. The sugar in the urine is galactose, and the babies cannot tolerate the galactose present in milk. In one case in which the patient died, examination of the liver showed periportal fibrosis, with atrophy of liver cells adjacent to the fibrosis and with large fat-containing vacuoles in the cells throughout the rest of the liver. When given a diet free of galactose (for example, "Nutramingen") the babies thrive.

Cystic Fibrosis of the Pancreas.

DOUGLAS E. JOHNSTONE AND ERWIN NETER (*Pediatrics*, April, 1951) state that one aspect of cystic fibrosis of the pancreas that is used to confirm diagnosis is the absence of trypsin in the duodenal contents and stool. It has been recommended that the presence of trypsin can be demonstrated in a stool by the ability of the stool to liquefy a gelatin film. The authors critically discuss this test. They state that it is well known that gelatin-liquefying organisms in the stool (for example, Proteus and Pseudomonas) may give false positive results. They carried out the test with 78 children suffering from cystic fibrosis of the pancreas, and found positive results in 48 cases. Gelatin-liquefying organisms were present in the stools of 44 out of 45 patients whose stools yielded a positive result from the gelatin film test; they were also examined bacteriologically. They were present in the stools of only two out of 28 patients whose stools yielded negative test results. In ten of the cases in which false positive test results were obtained, the duodenal juice was submitted to culture, and gelatin-liquefying organisms were found in all of them. Patients receiving penicillin had an increased incidence of these organisms in the stool. The authors state that the test is usually carried out with 1:5 and 1:10 dilutions of fæces in saline. A negative test result at such dilutions indicates an absence of trypsin and also of gelatin-liquefying organisms. The false positive results due to organisms can be excluded by further tests, including culture of the stool and repetition of the test with serial dilutions of stool and with soy-bean trypsin inhibitor. Treatment with pancreatin should be withheld for three days before the test.

Mercury and Pink Disease.

JOSEF WANKANY AND DONALD M. HUBBARD (*American Journal of Diseases of Children*, March, 1951) present in detail their suggestion previously made that exposure to mercury of hypersensitive children is the most important factor in the causation of infantile acrodynia. They state that exposure to mercury was demonstrated in 38 of 41 cases of acrodynia in children by the presence of the metal in their urine. In 23 of these cases mild mercurous chloride (calomel), teething powders or worm pills containing mild mercurous chloride, ammoniated mercury ointment and mercury bichloride used for rinsing diapers were ascertained to be the sources of mercury. Idiosyncrasy to mercury which manifests itself in acrodynia exists particularly in infants and small children, while older children and adults have a higher tolerance. Other factors which lower tolerance undoubtedly exist, but they are unknown at present. Hypersensitivity to mercury can manifest itself in many forms, and acrodynia is one of them. Acrodynia resembles recognized manifestations of mercury poisoning in many respects and differs from them in others. Transitional states exist between acrodynia and various established forms of mercury poisoning. It is possible that metals, drugs, and toxic substances other than mercury produce disease pictures resembling acrodynia. The effectiveness of dimercaprol (BAL) in the treatment of acrodynia could not be clearly demonstrated in the series of cases reported. It is possible that in cases of long standing the effect is not so striking as in cases of acute mercury poisoning.

Compression of Trachea or Œsophagus by Vascular Anomalies.

ROBERT E. GROSS AND EDWARD B. D. NEUHAUSER (*Pediatrics*, January, 1951) describe five types of vascular anomaly that may cause compression of trachea or œsophagus in the upper part of the mediastinum. They state that these malformations of the vascular system can give rise to difficulties in swallowing and to serious disturbances in pulmonary ventilation. The anomalies include double aortic arch, right aortic arch with a left *ligamentum arteriosum*,

anomalous innominate artery, anomalous left common carotid artery, and aberrant subclavian artery. The respiratory symptoms consist of crowing respiration, sometimes distressing dyspnœa, poor pulmonary ventilation with tendency to lung infection, and sometimes relief by extension of the head. The difficulty in swallowing is often not as distressing as the respiratory obstruction, but with an aberrant subclavian artery it may be the only symptom. There may be delay in swallowing, with some regurgitation. The symptoms may not be noticed until solids are taken, but are sometimes more pronounced with fluids. Radiological studies with lipiodol and barium show the indentation of trachea and œsophagus, and endoscopic studies may give useful confirmation. It is possible to attack surgically each of these vascular malformations. In general, the œsophagus or trachea can be relieved by division of an anomalous vessel or by displacement of an artery in such a manner that it is carried away from the compressed structure. When necessary, these operative procedures can be undertaken on very young babies, even in the presence of a high degree of respiratory obstruction. All the operations have been through a left antero-lateral, transpleural approach; general anæsthesia has been used with a closed system. The results of operation in 40 cases are analysed. The authors state that it is evident that many vascular anomalies in the thorax which disturb the functions of the œsophagus or trachea can now be treated with an excellent chance of relieving the obstructive symptoms.

ORTHOPÆDICS.

Spondylolisthesis with an Intact Neural Arch.

IAN MACNAB (*The Journal of Bone and Joint Surgery*, August, 1950) states that in spondylolisthesis the usual cause of anterior displacement of a vertebra is a bilateral defect in the *pars interarticularis*. Sometimes there is no such defect and the whole vertebra including the spine and neural arch is displaced forwards. He reports the clinical findings in 22 cases. He believes that the essential lesion is an alteration in angle between the pedicle and the inferior facet. The normal angle is about 90°, but in patients with spondylolisthesis with an intact neural arch the angle may be as much as 180°. When this increased angle is present the anterior dislocating force which occurs when the spine is flexed is resisted only by the soft tissues and mainly by the intervertebral disk. It is supposed that, because of the congenital alteration of angle, the abnormal strain eventually causes disk degeneration. When the disk degenerates the axis of movement passes through the posterior joints. This abnormal movement probably accounts for the gross osteoarthritis of the posterior joints seen in the later stages of the condition. It commonly produces a clinical picture of backache and sciatica, but the first effect may be "drop foot", and in unusual instances compression of the *cauda equina* may occur. Patients examined in the early stages who have no signs of nerve root compression are best treated by localized spinal fusion. Late fusion may afford no relief because of secondary changes in the spine, but these patients obtain some benefit from a corset. Laminectomy is indicated for severe symptoms in patients who have signs of nerve root compression; it should be followed by spinal fusion.

Hallux Valgus.

ROBERT J. JOPLIN (*The Journal of Bone and Joint Surgery*, October, 1950) states that a survey in 1947 of the end results of operations for *hallux valgus* at the Massachusetts General Hospital revealed that the Keller operation, employed for the most part up to that time, hardly gave satisfactory results. He believes that the Keller operation does not restore that degree of strength of the great toe which is essential to normal locomotion. It does not effect a significant correction of the mechanical faults that usually coexist in the foot as a whole. There is good evidence that it throws upon the rest of the foot a burden as great as, or even greater than, that imposed by the deformity for which the operation has been performed. Its value, therefore, is limited and is, in large measure, local. The author considered that it was advantageous to the *adductor hallucis*, as first suggested by McBride in 1928. He considered, however, that a better result would be secured if the tendon of this muscle was attached to some structure on the medial rather than on the lateral aspect of the first metatarsal. To prevent the *adductor hallucis* from suddenly overstretching, the long extensor tendon of the fifth toe was used to overcome temporarily the splay or spreading forces exerted by the soft tissues which had for years been adjusted to the deformity. Since October, 1947, this operation has been performed on 131 feet. The strength of the great toe, which is essential for normal locomotion or "take off", was not weakened. When considered as a whole, the foot appeared stronger. Most of the patients were able to wear a narrower shoe than formerly and to return to occupations requiring long periods of standing or walking. Varus of the great toe and splay foot were relieved in the majority of cases; arch supports and foot cuffs were usually discarded. The author gives a full description of the technique of the operation, which includes removal of any exostosis on the first metatarsal and tightening of the capsule on the inner side of the metatarso-phalangeal joint and also plastic repair on the fifth toe.

A Metallic Femoral Head.

LEONARD T. PETERSON (*The Journal of Bone and Joint Surgery*, January, 1951) has replaced the femoral head by a metallic prosthesis in ten hips. Six cases were unilateral and two were bilateral. In five of the six unilateral there was non-union of the femoral neck. Ankylosis due to rheumatoid arthritis was present in one unilateral case and in the two bilateral cases. The author states that osteotomy is performed through the subcapital region of the neck, the head is removed, and the acetabulum is reamed to its original depth. Only enough of the neck is removed to accommodate the device to be inserted, so that sufficient bone is preserved to support the metallic head and to maintain the original length. With the exception of one failure due to infection, the other nine hips in this series are all in active use. The steel femoral head has been well tolerated in the acetabulum, and there has been no evidence of necrosis or protrusion except in the one case in which infection developed. Except in that case, there has been no occasion to remove the head of the prosthesis or to expose the new joint. Minimal discomfort has been present, and there has been no evidence of pain due to the metal. There has been no bone necrosis due to pressure or traction nor any loosening of the screws. In one case with broken screws, a supporting ledge of bone has developed under the lower border of the plate, and the patient is bearing full weight without a cane. The author states that structural defects have led to fatigue fracture of one plate and of all screws in three cases. This indicates that the device should be strong and that proper technique should be observed in its application. It is possible to replace the plate and screws through a lateral approach to the femur without arthrotomy. The author has found that the minimum of post-operative care is required, active exercise is well tolerated, and full weight-bearing has been possible within three weeks. This device has furnished an effective means of arthroplasty or of reconstruction for non-union following fracture of the femoral neck.

Late Results in Legg-Perthes Disease.

EUGENE R. MINDELL AND MARY S. SHERMAN (*The Journal of Bone and Joint Surgery*, January, 1951) have studied the end results of treatment of 72 patients with 78 hips affected by Legg-Perthes disease. Half were followed for six to fifteen years; six individuals were followed for over twenty-five years. The authors state that the prognosis in a case of Legg-Perthes disease can in a general way be estimated early in its course. Younger patients have been shown to have a higher incidence of satisfactory results. In the natural course of Legg-Perthes disease there is a wide variation in the severity of the process. Pronounced changes in the femoral neck and lateral expansion or central depression of the femoral head indicate a bad prognosis. Premature symmetrical or asymmetrical growth arrest of the capital femoral epiphyseal cartilage plate may occur and contribute to the deformity. In the presence of gross changes on the radiographs there may be few or no symptoms in early adult life. However, as the patient becomes older, progressive disability does occur. The authors consider that inasmuch as no significant difference is found in the results from non-ambulatory and ambulatory methods of treatment, the latter is the treatment of choice when the disease is unilateral. Occasionally, when the initial symptoms and findings are pronounced, bed rest or traction for a week or two is beneficial. However, complications do occur from prolonged bed rest and immobilization. The use of crutches avoids these complications and permits a fairly normal existence. For the younger child, a halter attached to the shoe maintains knee flexion; only rarely is it necessary to provide more restriction or to admit an uncooperative patient to hospital.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at the Alfred Hospital, Melbourne, on May 16, 1951. The meeting took the form of a series of clinical demonstrations by members of the honorary medical and surgical staff of the hospital.

The Use of Cortisone in Type II Nephritis.

DR. DONALD G. DUFFY presented two patients with type II nephritis to whom cortisone had been administered during the phase of generalized œdema. The first patient was a woman, aged forty-eight years, who had first presented with generalized œdema and gross albuminuria in 1938. There was a past history of scarlet fever in infancy and puerperal sepsis fourteen years previously. Examination revealed albuminuria, a blood pressure of 140 millimetres of mercury (systolic) and 80 millimetres (diastolic), no retinal changes and normal renal function test results. During four months spent by the patient in hospital, abdominal paracentesis was performed on twelve occasions, and after her discharge from hospital it was performed at weekly intervals until her second admission to hospital in a grossly œdematous state two months later. From that time onwards until 1946 the patient had spent three months of every year in hospital with generalized œdema and ascites which required repeated tapping. Albuminuria persisted, while the level of blood pressure and results of renal function tests remained normal. The serum albumin content was maintained in the region of 1·6 grammes *per centum*. Since 1946 the patient had been admitted twice to hospital at intervals of three and two years respectively, the most recent being in March, 1951. Her blood pressure on that occasion was still in the region of 140 millimetres of mercury (systolic) and 90 millimetres (diastolic), the serum protein content was 3·9 grammes *per centum*, made up of albumin 1·5 grammes *per centum* and globulin 2·4 grammes *per centum*, and there was pronounced albuminuria. In view of the difficulty previously encountered in initiating diuresis in this case, it was decided to administer cortisone after a week during which her œdema increased despite salt restriction and "Neptal" injections. "Cortone" was accordingly administered in an initial dose of 300 milligrammes on the first day, followed by 200 milligrammes on the second day and 100 milligrammes on subsequent days. The drug was given in "divided" doses over a period of two weeks. During its administration the patient felt extremely well and, contrary to her usual custom at that phase of the disease, maintained her appetite and was not nauseated. Her œdematous state, however, remained, and in fact her ascites increased considerably towards the end of the fortnight of cortisone administration. Because of her discomfort *paracentesis abdominis* was then performed, following which diuresis occurred and her œdema subsided. Dr. Duffy said that the necessity for this interference was unfortunate, since it obscured the responsibility for the subsequent diuretic response which had been observed to occur upon the cessation of cortisone or ACTH administration, or might have been initiated, on the other hand, by the removal of ascitic fluid.

Dr. Duffy's second patient was a man, aged thirty-eight years, who had been admitted to hospital for the first time in December, 1950. The onset of generalized œdema had been noted a week prior to his admission to hospital, together with headache, anorexia, nausea and vomiting. There was no past history of renal disease. Examination of the patient revealed œdema of legs, thighs, abdominal wall and face, ascites, gross albuminuria and a blood pressure of 120 millimetres of mercury (systolic) and 85 millimetres (diastolic). Microscopic examination of urine showed the presence of granular casts, but no red blood corpuscles. The serum protein level at this stage was 3·4 grammes *per centum*, made up of albumin 2·3 grammes *per centum* and globulin 1·1 grammes *per centum*. Treatment was commenced with restriction of salt intake to one gramme per day and intramuscular injections of "Neptal" two millilitres on alternate days, but this did not prevent the further accumulation of œdema. Acupuncture was performed thirteen days after the patient's admission to hospital, and above ten pints of fluid were drained from the legs during the next three days. The patient then became nauseated owing to salt depletion, and the serum protein value was then 3·2 grammes *per centum* (albumin 1·6 grammes *per centum*, globulin 1·6 grammes *per centum*). His œdema reappeared rapidly, and one litre of dextran solution was administered in an endeavour to raise the intravascular osmotic pressure. This produced a transient diuresis, but a further litre of dextran given three days later was ineffectual in this regard. Acupuncture was again performed, and the loss of over ten pints of fluid from the legs was again accompanied by nausea and vomiting. Subsequent recurrence of œdema was treated by the induction of pyrexial episodes with T.A.B. vaccine and the intravenous administration of one and a half litres of "Parenamine", but again without success. Acupuncture became necessary in view of his breathlessness and pitting œdema to the level of the nipples. Dr. Duffy said that a course of cortisone was then given similar in dosage and duration to that described for the previous patient. During the exhibition of the cortisone, the œdema increased while the amount of albumin excreted daily in urine was much increased as well. Despite the increased albuminuria the serum albumin remained at the same level of 1·3 grammes *per centum*. There was considerable subjective improvement in the patient's sense of well-being, loss of nausea and increased appetite for all foodstuffs. That improvement was noticed in both cases and was maintained after cessation of cortisone therapy. Four days after cortisone administration was discontinued, the accumulation of œdema necessitated acupuncture, and two days later a litre of plasma was administered. The œdema began to diminish three days later without any alteration in the serum albumin level.

Dr. Duffy said that these two cases of type II nephritis under discussion, one long standing and the other recent, had appeared to follow a similar course following cortisone administration. There was no coincidental diuresis, but rather an increase of the œdema during the course and diuresis some days after cessation of therapy. Albumin excretion was increased when cortisone was administered, while the patients exhibited a subjective sense of well-being resembling that observed by patients with rheumatoid arthritis treated with that drug. The two cases, while inconclusive in themselves, pointed to the necessity for further observation upon the changes induced in the secretion of antidiuretic hormone during and after cortisone administration. While it was unlikely that cortisone administration would alter the fundamental changes in the glomerular capillaries and so change the course of the disease, it would appear probable that its use during the phase of generalized œdema would in some cases initiate diuresis. The mechanism by which that was brought about was not certain, but it might relate to an alteration in the secretion of antidiuretic hormone by the pituitary. It was obvious that the level of serum albumin alone had little to do with either the accumulation or the loss of the œdema fluid.

Traumatic Rupture of Abdominal Viscera.

DR. ROBERT S. LAWSON showed a series of twelve patients who had sustained rupture of the spleen, kidney, liver, bowel or bladder from non-penetrating injuries. The various mechanisms of injury and the cardinal features in diagnosis were discussed. Examples of splenic rupture from apparently trifling injuries were demonstrated, notably in children. Attention was drawn to the combination of hæmothorax with ruptured spleen and left kidney occurring in pedestrians struck by motor vehicles. One patient in the series, aged fifty-two years, had survived those injuries after treatment by splenectomy and left nephrectomy.

Asthma.

The staff of the Asthma Clinic showed patients to illustrate methods of investigating and treating asthma.

DR. J. ALEXANDER discussed the management of children who were intolerant of cow's milk. He said that in some cases boiling altered the milk sufficiently, in others it could be modified by the addition of lactic acid, and in a few cases it was necessary to eliminate cow's milk and use goat's milk or soy-bean emulsion. He also discussed the management of children in whom allergy and infection seem to combine in precipitating asthmatic attacks. Control of the allergic aspect frequently lessened a tendency to develop head colds.

DR. PAUL WARD FARMER showed two patients to illustrate the eczema-asthma sequence. Both had had severe eczema in early infancy and had developed asthma at about the age of twelve months. The first, aged nine years, had shown intense sensitivity to horse dander, house dust, pollen and egg white and other foods two years previously, but recent tests showed that the intensity of many reactions had

diminished. House dust and egg white still caused strong reactions, but the patient showed great clinical improvement after a course of desensitizing injections.

The second patient, aged seven years, had reacted to many pollens, foods and dusts including kapok. Improvement had followed avoidance of kapok and a course of non-specific therapy with a stock vaccine. Dr. Farmer emphasized the advisability of actively immunizing horse-sensitive patients by giving tetanus toxoid to obviate the use of tetanus antitoxin.

DR. ALAN MURRAY showed two patients. The first was a woman who had suffered with spring hay fever for the past twelve years, most pronounced in August. Skin tests showed strong sensitivity to elm tree pollen and smaller reactions to grass pollens. She had had two courses of injections of a mixed pollen extract with much benefit.

Dr. Murray's second patient was a pastrycook, who was sensitive to wheat flour. Treatment by desensitization had been started, but an intradermal test still showed very pronounced sensitivity to wheat, indicating that he would require prolonged treatment.

DR. CHARLES SUTHERLAND showed three patients with asthma, including a man, aged twenty-one years, who for the past four months had suffered from attacks of intense hay fever and asthma when handling rabbit fur. The patient noted that only furs infected with weevils upset him, and an extract of this weevily rabbit fur produced a large reaction on his skin. This extract when tested on ten other asthmatic subjects produced no reaction in eight and a faint flush in two cases. Treatment by desensitization had commenced. The new allergen was heat-stable and was not toxic to mice.

In answer to questions, precautions when associated with the giving of potent extracts of allergens were discussed. In dealing with asthmatic children, it was emphasized that infection was even more important than allergy, and that in some children attacks could be effectively controlled by brief courses of sulphonamides or antibiotics.

Ophthalmic Demonstration.

DR. W. M. BOX and DR. H. H. JOHNSON showed a series of patients with ophthalmic conditions.

Two patients with *retinitis pigmentosa* had the typical picture of night blindness, gross concentric constriction of visual fields, retinal pigmentation and optic atrophy. One patient had had a cervical sympathectomy performed on one side ten years previously without any improvement in the condition.

Two patients with spring catarrh were shown. Besides the palpebral lesions, they were under treatment for asthma and eczema.

Four patients with diabetic retinopathy were demonstrated. They had the typical diabetic hæmorrhages and exudates.

A man, aged forty years, was shown with a left-sided pulsating exophthalmos of traumatic origin, due to a carotid cavernous sinus fistula. The common carotid artery on that side had been ligated with some reduction in the signs. Optic atrophy had supervened. Diplopia and restricted ocular movements were present.

A male patient, aged forty years, with *retinitis circinata* was shown. The *retinitis circinata* had been seen to develop over a period of eighteen months. The patient had developed thrombosis of the right superior temporal branch of the right retinal vein three weeks after an operation for hæmorrhoids. A sector-shaped area of hæmorrhages had first been evident, and the present picture had gradually supervened.

Modification of the Macintosh Oxford Inflator.

DR. DOUGLAS G. RENTON demonstrated a modified Macintosh Oxford lung inflation apparatus for anæsthesia. He said that the original Oxford apparatus required the use of both the anæsthetist's hands, one to manipulate the bellows and the other to control the exhale valve or orifice. In the modified edition, control of exhalation was automatic, and one hand operated the bellows and exhale mechanism.

X-Ray Appearances in Œsophageal Lesions.

DR. B. L. DEANS had prepared films illustrating radiological appearances in various lesions of the œsophagus. In his absence, because of illness, these films were demonstrated by Dr. H. A. Luke.

A MEETING of the New South Wales Branch of the British Medical Association was held on May 24, 1951, at Royal Prince Alfred Hospital, Camperdown. The meeting took the form of a series of clinical demonstrations by members of the honorary medical and surgical staffs of the hospital.

Multiple Myeloma, Radiologically Simulating Cysts in Bones.

DR. J. H. TYRER presented a man, aged twenty-nine years, who had been admitted to hospital in April, 1950, with severe pain in the left side of the abdomen, radiating to the back. While in hospital he had at first much lumbo-sacral pain, and pain radiating into both thighs. X-ray examination revealed a wedge-shaped deformity of the first lumbar vertebra, the possibilities considered being a congenital deformity, an old fracture or a destructive lesion. The patient was discharged from hospital for two weeks, walking in a plaster jacket. On his return to hospital, pain was still present, and the plaster jacket was removed. Clinically, his radial arteries were palpable, his blood pressure was 165 millimetres of mercury, systolic, and 120 millimetres, diastolic, while a tender swelling was apparent below the left iliac crest. X-ray examination revealed a cystic area in the left iliac crest, and also widely disseminated areas of bone transradiance, up to three or four centimetres in diameter, in certain bones, clearly arising in the marrow and eroding into the cortex, with no surrounding osteal or periosteal reaction. The skull, pelvis and long bones were heavily involved. Blood calcium, phosphorus and alkaline phosphatase levels were normal, the blood protein content was 8·25 grammes *per centum*, while the blood urea content was 74 milligrammes *per centum*. Examination of the urine revealed scanty cellular and hyaline casts and a heavy cloud of Bence-Jones proteose. The patient developed a progressive secondary anæmia, and examination of the blood showed heavy rouleaux formation. The result of sternal marrow biopsy was not diagnostic, but Dr. Edgar Thomson reported that there were plasma cells present in numbers greater than those usually seen in marrow, but that they were not the predominant cell; the appearances could be compatible with a myeloma.

Dr. Tyrer said that over the past ten months the patient had become progressively paler and had had many blood transfusions; the bone pains had recurred in the back, thighs, pelvis, shoulders and skull; he had lost about four stone in weight and had become progressively weaker. He had had two short courses of stilbamidine. During the last month the liver and spleen had become palpable.

Localized Fibrocystic Disease of Bone.

Dr. Tyrer's second patient, presented as a contrast to the first, was a boy, aged thirteen years. In 1948 he had fallen during a game of football and fractured the upper part of his left humerus. X-ray examination at that time showed a "bone cyst" at the site of the fracture. His left arm was kept in a sling for several weeks, and the fracture healed. Subsequent X-ray examination showed persistence of the cystic area in the left humerus, but no other "bone cysts". In May, 1951, the patient was admitted for the first time to the Royal Prince Alfred Hospital. Clinically, some deformity of the left humerus at the site of the old fracture was still apparent. X-ray examination showed a healed fracture and loculated fibrocystic disease involving about seven centimetres of the upper part of the left humerus. X-ray examination of all other bones revealed no abnormality. The blood calcium, phosphorus and alkaline phosphatase values were normal, as also were the blood urea, cholesterol and lipoid values. A full blood count revealed no abnormality and the result of a Casoni test was negative.

Patent Ductus Arteriosus and Coronary Artery Disease.

The third patient presented was a man, aged forty-nine years, who had been told in 1922, after a routine examination, that he had a "heart murmur". He had had no cardiac symptoms until 1945, when he noticed moderately severe substernal pain on exertion, relieved by rest. In July, 1948, the patient "fainted" one morning and was unconscious for about twenty minutes. Since then he had had four similar fainting turns, the substernal pain on exertion had become worse, and breathlessness on exertion had appeared. In April, 1951, he was admitted to hospital. Clinically his radial arteries were palpable, his blood pressure was 125 millimetres of mercury, systolic, and 60 millimetres, diastolic. The cardiac apex beat was displaced to the left, and a continuous "machinery" type of murmur was heard over the second

left intercostal space, close to the sternum. An X-ray examination of the chest revealed considerable cardiac enlargement, principally due to enlargement of the left ventricle, and also the suggestion of a small calcified plaque in the aortic knob. Electrocardiograms showed left bundle branch block and a prolonged *P-R* interval. Discussion at the meeting centred on the advisability of surgical treatment for the patent *ductus arteriosus*.

Tumour of the Left Cerebral Hemisphere.

The fourth patient was a man, aged thirty-seven years. Commencing in September, 1950, he had had gradual onset of right hemiplegia, beginning as apraxia of the right hand, followed by progressive weakness of the right upper and then the right lower limb. In November, 1950, it had been observed that the right hemiplegia included lower right facial weakness and there was also almost pure motor aphasia. By February, 1951, the results of extensive investigations (examination of cerebro-spinal fluid, charting of visual fields, plain X-ray examinations of the skull, intracranial angiography, ventriculography and needle exploration of the cerebrum through burr holes, blood Wassermann and Kline tests) were all normal, with the sole exception of the electroencephalogram, which suggested a focal lesion in the left temporal region. By May, 1951, the patient's condition had become worse; his vision had deteriorated and there was bilateral papilledema; instead of almost pure motor aphasia the patient then confused simple instructions such as "Put out your tongue". The left foot, as well as the right, showed an extensor plantar response. The hemiplegic right side was at times quite hyperalgesic and hyperæsthetic, and it had been suggested that the lesion might be irritating the thalamus. Examination of cerebro-spinal fluid showed a pressure exceeding 275 millimetres of cerebro-spinal fluid, and 18 lymphocytes per cubic millimetre. The electroencephalogram suggested a left temporo-parietal lesion, though clinically the signs were more in favour of a left fronto-parietal lesion.

Hepatic Cirrhosis and Possible Ulcerative Colitis.

Dr. Tyrer's last patient was a woman, aged thirty-eight years. For the past four years she had had diarrhœa, with about six to eleven loose motions daily, often containing dark red blood; defæcation had been associated with lower abdominal pain and tenesmus. Six weeks before admission to hospital she had begun to feel tired and lethargic; she noticed upper abdominal pain, anorexia, nausea and vomiting, felt feverish, and a few days later noticed that her skin was yellow, her urine was dark and her fæces were pale. There was no history of alcoholism or previous history of jaundice. After her admission to hospital on May 14, 1951, clinically there was a slight icteric tinge to the conjunctivæ, though that disappeared in a few days. The liver and spleen were readily palpable, there were numerous spider nævi on the chest, neck and upper limbs, while the reddened thenar and hypothenar eminences suggested the so-called "liver palm". One week after her admission to hospital the serum bilirubin content was two milligrammes *per centum*, the result of the serum thymol turbidity test was expressed as "++++" and the serum alkaline phosphatase content was 22·8 King units. Examination of the stools showed no cysts, ova, amœbæ or parasites, and on culture *Bacterium coli* was grown. Liver biopsy revealed well-marked portal cirrhosis. Sigmoidoscopy at this time showed slight mucosal injection but no ulcers, pus or excess mucus. X-ray examination with a barium enema showed no haustrations below the left flexure of the colon, and the appearance was consistent with colitis. There was discussion at the meeting on the possible relationship of portal cirrhosis and colitis.

Carcinoma of the Lung.

DR. A. F. GRANT presented a man, aged forty-three years, who had been admitted to hospital on April 6, 1951, with the complaint that two or three months before admission he had become very tired and drowsy; also he noticed a dull ache in the chest, especially on the right side. He had had a slight cough for some years, but that had ceased since he gave up smoking one month before his admission to hospital. He had never had hæmoptysis, hoarseness or dyspnœa and X-ray examination of the chest showed a lesion in the upper lobe of the right lung which was suspected by his own doctor of having been tuberculosis. Sputum examination did not reveal acid-fast bacilli, and further X-ray examination showed a partial atelectasis of the upper lobe of the right lung which was not unlike the condition seen in tuberculosis. Bronchoscopy was performed on March 28 by Dr. H. M. Rennie and showed a tumour growing out of the right upper lobe bronchus. This was subjected to biopsy, but the report was "granulation tissue". The results of examination of bronchial washings were negative for carcinoma cells. On May 7 right pneumonectomy was performed by Dr. J. S. MacMahon, and the patient made an uneventful recovery. The pathologist submitted the following report on the lung removed:

> Macroscopic: The specimen showed a small tumour in the mouth of the right upper lobe bronchus which did not extend outside the bronchus wall any further than 1 mm. Beyond the carcinoma the upper lobe was found to be atelectatic in the anterior segment with dilatation of the bronchi.
>
> Microscopic: Squamous carcinoma with keratin formation. No carcinoma in the regional lymph glands. The carcinoma is very superficial and has not penetrated the bronchus far.

Dr. Grant's second patient, a man, aged fifty-seven years, had been admitted to hospital on February 20, 1951. His history was that in December, 1950, he had noticed that he was becoming more tired, but he had put that down to worry at work. Over a period of six weeks he had lost about half a stone in weight, and three weeks before his admission to hospital he coughed up a teaspoonful of blood. Two weeks prior to his admission to hospital he had noticed a dull ache in the anterior part of his chest on the left side on deep breathing or coughing. An X-ray picture taken at work had shown a mass in the left lung which was round, but its contour was not sharp. It was well away from the hilum. He had had a cough with a small amount of sputum for many years and smoked about three ounces of tobacco per week. Investigation of his past health showed that in 1917 he had had pneumonia and pleurisy, and during that illness had coughed up blood and some grapeskin-like material which was diagnosed as hydatid cyst. X-ray examination in 1938 had shown a calcified hydatid cyst of the liver. On March 2, 1951, bronchoscopy was performed by Dr. H. M. Rennie. The left main bronchus was slightly congested, but no other abnormality was found. Examination of bronchial washings showed no carcinoma cells. The result of a Casoni fixation test was negative, but the result of a Casoni test was positive, immediate and delayed. On March 12 a left thoracotomy was performed by Dr. J. S. MacMahon. The upper lobe was found to be adherent in a circumscribed area to the parietal pleura. Left upper lobectomy was performed, and the patient made an uneventful convalescence. The pathologist submitted the following report on the tissue removed:

> Macroscopic: A small carcinoma was found in the anterior segment bronchus of the upper lobe. Distal to this there was a segment of fibrosis and atelectasis of the lung and this atelectasis was the shadow seen in the X ray.
>
> Microscopic: The tumour is an adeno-carcinoma becoming anaplastic in places and in some places it is simulating alveolar architecture. The lymph glands were not involved.

Dr. Grant then presented a man, aged fifty-six years, who had been admitted to hospital on March 8, 1951. The patient stated that he had developed a cough approximately three years previously, which was worse in the mornings and seemed to be more severe during the winter months. The cough was irritated by smoke, and he produced clear gelatinous mucus which was never blood stained. Periodically after exertion over the last two years he had noticed a sharp severe pain in the chest on the left side anteriorly. Since that time he had had periodic X-ray examinations, which had shown the lesion in the left lung, and he was referred to the Royal Prince Alfred Hospital in January, 1951. X-ray examination showed a lesion in the middle zone of the left lung extending out from the mediastinum almost to the periphery. No definite mass was seen in the X-ray film, and a lateral view showed what appeared to be a small segment of collapsed lung. A bronchogram showed that the lipiodol would not fill the anterior portion (pectoral segment) of the upper lobe. Bronchoscopy was performed on March 14 by Dr. H. M. Rennie, and the mucosa of the left upper lobe bronchus was reddened and irregular, but no definite evidence of neoplasm was found. Bronchial washings were taken, but examination of these did not show carcinoma cells. It was decided that a left thoracotomy should be performed, and on April 9 left pneumonectomy was performed by Dr. J. S. MacMahon. At operation the

upper lobe was found to be adherent in the anterior segment, and there were some large glands at the hilum. Examination of a frozen section of one of these glands showed inflammatory changes but no carcinoma. The patient made an uneventful recovery. The pathologist made the following report on the excised lung:

> Squamous cell carcinoma of the left upper lobe bronchus which is fairly anaplastic. No involvement of the hilar lymph glands noticed.

Hydatid Cyst of the Lung.

Dr. Grant's next patient, a youth, aged sixteen years, had been admitted to hospital on March 8, 1951. It was stated that he had been quite well until the night of March 4, when, while boxing, he was struck on the right side of the chest and soon afterwards began to cough and produced sputum streaked with blood. That staining of the sputum had persisted, and the night before his admission to hospital he had brought up half a cup of bright blood. Investigation of his previous history showed that he had spent much time in his life on the Southern Highlands. Blood examination revealed a hæmoglobin value of 13·3 grammes *per centum* and a total leucocyte count of 7400 per cubic millimetre, 4% being eosinophile cells. The Casoni test produced an immediate positive reaction and a delayed negative reaction. The result of a hydatid complement-fixation test was positive. X-ray examination of the chest showed that there was at least one, and possibly two, large cystic areas in the right lung with a fluid level. Examination of a lateral view confirmed the presence of a single large cavity with a fluid level in the right lung anteriorly. On March 15 a right thoracotomy was performed by Dr. J. S. MacMahon. A segment of the right fifth rib was removed in the anterior region, and a large hydatid cyst of the upper lobe which was not adherent to the parietal pleura was found. This was opened, a large laminated membrane was removed, a tube was inserted and the edge of the ectocyst was stitched to the edge of the wound, the lung being kept expanded by positive pressure. A large bronchial fistula was present which retarded convalescence. X-ray examination on May 18 showed that the adventitious cyst was only half the previous size. The patient at that time was very well and had only a slight, dry cough.

Neuroblastoma of the Lung.

Finally, Dr. Grant presented a boy, aged eight years, who had been admitted to hospital on April 18, 1951. The history was that during January, 1951, the patient had become feverish and irritable and had pains all over his body. Several days later the fever had abated, but the child had become paralysed in the back, left arm, right leg and right foot, and had some paresis of the neck and abdomen. Poliomyelitis was diagnosed, and the boy was transferred to Prince Henry Hospital for five or six weeks, during which time he made a fairly satisfactory recovery. He was then transferred to Western Suburbs Hospital for physiotherapy, and while there had an attack of pain in the chest, dyspnœa and pain in the back, high up. X-ray examination of the chest showed a mass in the superior mediastinum on the left side. The attacks of breathlessness and pain disappeared, and the child was admitted to Royal Prince Alfred Hospital, symptom free. Three days before his admission to Royal Prince Alfred Hospital a bronchoscopy had been performed at Western Suburbs Hospital, which revealed no abnormality, and a biopsy was also taken from a lump in the neck which was believed to be a lymph gland. A section was sent to Royal Prince Alfred Hospital and was reported on by Dr. V. J. McGovern as poorly differentiated ganglioneuroma. Investigation of the past history revealed that since the patient's birth his parents had noticed that if he became excited or overheated, flushing on the right side of the face and neck only was observed. Mantoux tests, Casoni tests *et cetera* gave no help. On May 7 a left thoracotomy was performed by Dr. J. S. MacMahon and a large mass in the anterior mediastinum was observed. This was of rubbery hardness, but seemed to be a secondary deposit from a tumour in the posterior part of the mediastinum which was slightly smaller than the secondary deposit. Also an extension along the fourth left intercostal bundle was noticed, and there was a large gland present at the hilum of the lung which seemed of the same consistency as the rest of the tumour. Biopsy was taken from the secondary tumour and two biopsies from the intercostal extension, and these proved to be neuroblastoma with some differentiation towards ganglioneuroma. The child was to receive deep X-ray therapy.

(To be continued.)

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

SURGEON BALMAIN TO GOVERNOR HUNTER.[1]

[*Historical Records of Australia.*]

Sydney,
N.S.W.,
1st August, 1798.

Sir:

Enclosed is a state of the sick continued from the 31st of July, 1797, to the 31st of July last, together with a copy of the last demand of medicines and necessaries for the use of the hospital under my direction and also a fresh demand for various other articles, which are much in use and almost quite expended.

It will scarcely be necessary for me to request that you will be pleased to represent the propriety of a punctual attention to these demands, as you must be perfectly aware of the inconveniences which must arise from the want of all or any of them.

It is also my duty to state to your Excellency that the extent of our detachment requires a greater number of assistant surgeons, and that for want of them much inconvenience is felt by the inhabitants.

I have on a former occasion represented to you that an unskilled convict performs the medical duty at the Hawkesbury, a numerous and extensive settlement. One assistant surgeon is stationed at Norfolk Island and no person with him capable of taking his charge in case of accident or ill health. Another of the gentlemen is placed at Parramatta, a populous place, where constant watchfulness and attention is required and myself with two others perform the duties at head-quarters. From this statement I hope it will be evident that the number of medical men is far too small, and that in addition to the assistant promised in the room of the late Mr. Irwin another assistant surgeon, together with an apothecary for the hospitals, are indispensibly necessary.

If what I have taken the liberty to observe on this subject be approved of, an assistant surgeon may be spared from headquarters, as the apothecary will fully supply his place, and have also time to perform his own particular duty. By this arrangement there will be five assistant surgeons on detachment, which I think will in the present state of the colony be sufficient.

Men of abilities should be selected for the most obvious reasons, and here I beg leave to recommend Mr. Thos Arndell to the appointment of apothecary: he is in every respect well qualified for the office, and as he enjoys a pension of £50 pr annum for his past services as an assistant surgeon, would be well satisfied to do the duty by having his pay made up to that of an apothecary.

With submission to your Excellency's judgement and opinion.

I have, &c.,
W. BALMAIN.

Correspondence.

DICOUMAROL IN THE TREATMENT OF CORONARY OCCLUSION.

SIR: In regard to Dr. Whishaw's excellent and purposeful paper on the above subject, I suggest that his conclusions would have found an even happier note with better laboratory control.

Before pursuing this somewhat pontifical statement further, I quote from his paper: "Owing to the wide variation of individual response, no standard dosage could be employed, and it was found to be difficult and sometimes impossible to keep the prothrombin index in the region of 25%, the ideal figure. Whether or not this is important is undecided, and in the present small group of patients no conclusion on this point could be drawn."

[1] From the original in Mitchell Library, Sydney.

I assume that Dr. Whishaw did not have at his disposal a prothrombin activity assessment that took into consideration the newly recognized accelerator substance, variously termed, according to methodology or terminology, Owren factor V, Quick's component A, accelerator globulin (Fantl and others), serum prothrombin conversion accelerator *et cetera*. The discovery of this fifth clotting factor in recent years "has offered a possible solution to some of the erratic results following dicoumarol administration", and has rendered the derisive observation that there are more theories of blood coagulation than investigators less pertinent and colourful. One gathers the impression, as a result of a visit to Professor Owren at Oslo, and subsequently through America, that anticoagulant therapy will not be on a secure basis without reference to the known amount of accelerator globulin; a patient with a low prothrombin and high accelerator globulin activity will be very susceptible to dicoumarol, as shown by Olwin, Ware and Seegers in the two-stage method, which provides safer control of prothrombin during dicoumarol therapy. Ware now has adopted the prothrombin-free plasma method as practised by Owren and finds this control adequate. Marple and Irving Wright, of Cornell University, New York, use the Link-Shapiro method, a modification of Quick, and it will be interesting to see if this renowned group revise their methods as time goes on.

To quote again from Dr. Whishaw's paper: "A study of the prothrombin indices confirmed the fact that in some persons the action of dicoumarol was prolonged for a week or more after it had been discontinued." It has been noted by Olwin that accelerator globulin values fell during the early days of dicoumarol treatment and did not return to normal for some twenty-one days after, thus again pointing to the necessity of adding a measured amount of accelerator globulin in the assessment of prothrombin activity. It is therefore likely that the seemingly prolonged action of dicoumarol that Dr. Whishaw found was due to this factor.

The occasion seems an appropriate one to ventilate this vexed question of the anticoagulant drugs in the treatment of coronary heart disease, and one is further prompted to do so after reading Dr. C. G. McDonald's Listerian Oration in the last issue of THE MEDICAL JOURNAL OF AUSTRALIA, wherein he carries the torch so effectively for the doctor and his art.

In these days of beneficent governments ever ready to open our purse-strings for pharmaceutical benefits, it is little short of a horror to reflect that expensive and dangerous drugs, such as heparin and dicoumarol, are available for general use. If, on the one hand, they are used by the uninitiated in a dosage to be effective, it is comparable to handing the controls of an aeroplane in mid-air to a person who has never flown before with an injunction to "Go ahead, it's all yours"; if, on the other hand, these drugs are used as a harmless gesture to placate and impress the patient and his friends, it is both craven and dishonest.

Finally, given suitable laboratory control, the weight of evidence overseas is such as to suggest that the coronary atherosclerotic with past or impending coronary occlusion is, in many instances, benefited by the anticoagulant drugs.

Yours, etc.,
W. J. McCRISTAL.

Sydney,
June 23, 1951.

A MORE REALISTIC VIEW OF TUBERCULOSIS.

SIR: I should like to add to my letter that was published in the issue of the journal of April 7, 1951 (page 529).

As regards my criticism of mass radiography, my objections are concerned with methods rather than principles. At the present time, there are numerous organizations dabbling in tuberculosis, its diagnosis and treatment, its publicity, and financial assistance to those concerned. These include the State and Commonwealth Departments of Health, the Joint Coal Board, the Repatriation Department, workers' compensation, the Tuberculosis Association and the Anti-Tuberculosis Association, district and general hospitals, private general practitioners and specialist practitioners. There is naturally a good deal of reduplication and waste (particularly in X-ray work) with resulting overlapping, confusion and conflicting reports.

It is quite inadequate for a travelling clinic to wander through the State, and like a travelling circus pitch camp where the "takings" are likely to be worth while, and then, passing on, leave a few worried people to be further investigated. The practice of X-raying children in such surveys, without first doing a tuberculin sensitivity test, may be of some satisfaction to aldermen and parents, but has little else to recommend it. The minimal lesion is not easily detected on a standard postero-anterior film, even if of full size. A lordotic view is essential to locate many of these lesions.

The only sensible way to tackle the problem is to have a series of fully equipped and staffed clinics in central locations. These clinics would be able to do radiography (including interpretation), sputum testing, sensitivity testing, B.C.G. vaccinations, and artificial pneumothoraces. They would follow up the cases fully as regards their health, housing conditions and contacts. The obvious place for such clinics is in the district hospitals in the country, and the general hospitals in the cities. If the hospitals are incapable of such expansion, separate clinics should be established. This method would ensure the essential continuity of follow-up and would be invaluable, not only in controlling the disease, but also in filling the gaps in our knowledge as regards its natural course.

In this age of specialization, the average private medical practitioner has neither the experience nor the desire to do anything more for the tuberculosis suspects than refer them for radiological opinion (which is often based on the interpretation of a single film).

The question of resistance to tuberculosis infection is naturally most important. There is a widely accepted belief that Europeans have built up an inherited resistance to the disease. This presumes that the less resistant types have gradually been reduced by the survival and breeding of the more resistant survivors. This is naturally an attractive supposition (to the Europeans at least!). Tuberculosis is rife in war-devastated Europe, where both nutrition and housing have deteriorated. This is a well-known fact, and we do not need to postulate any racial or constitutional factor to account for it. Tuberculosis in Australia is relatively uncommon (that is, progress reports on the survey in Tasmania); our background, as regards nutrition, housing and weather, is correspondingly better than in Europe. If we believe that resistance lies in previous infection or B.C.G. vaccination, we could vaccinate with B.C.G. as we now vaccinate against a threatened outbreak of smallpox.

The explanation, of course, could be much simpler: it is generally accepted that tuberculosis is less rife amongst the better nourished and housed members of the community. In Australia at least, the policeman and professional football player type seldom get tuberculosis, or if they do get it (routine X-ray diagnosis), they usually seem to have sufficient resistance to overcome it. The Papuan native, the Australian aboriginal and other native races succumb to tuberculosis very quickly. They also appear to succumb readily to other infections including indigenous ones (with a few exceptions, such as local strains of the malarial parasite). Their expectation of life, even without outside contact, is probably small, and their diet is, generally speaking, poor as regards "protective" foodstuffs, regular meals, and, of course, their housing and sanitation is generally very poor. These facts are common knowledge, but their implications seem to be largely overlooked.

Yours, etc.,
B. SHORT.

Cessnock,
New South Wales,
June 13, 1951.

The Royal Australasian College of Physicians.

SIMS COMMONWEALTH TRAVELLING PROFESSOR, 1951.

AN invitation is extended to all members of the medical profession to attend the following lectures to be given by Dr. D. M. Dunlop, Sims Commonwealth Travelling Professor for 1951.

Lectures in Hobart.

Dr. Dunlop will deliver the following lectures in the library of the Royal Society, Tasmanian Museum, Argyle Street, Hobart:

Tuesday, July 31, 1951, 8.15 p.m.: "The Status of Therapeutic Dietetics in Medicine."

Friday, August 3, 1951, 8.15 p.m.: "The Effect of the Endocrine Glands on the Skin."

Lectures in South Australia.

Dr. Dunlop will deliver the following lectures in the Verco Theatre, Royal Adelaide Hospital, Adelaide:

Friday, August 10, 1951, 8.30 p.m.: "Antihistamine Drugs."

Tuesday, August 14, 1951, 8.30 p.m.: "Changing Fashions in Medicine."

Thursday, August 16, 1951, 8.30 p.m.: "Thiouracil."

He will also deliver one lecture at Hamley Bridge on Sunday, August 12, 1951, at 2.45 p.m., on the subject "Some Medical Aspects of Obstetrics and Gynæcology".

Lectures in Perth.

Dr. Dunlop's lectures in Perth will be delivered in the university lecture theatre, Perth, on the following dates:

Friday, August 24, 1951, 8 p.m.: "The Effect of the Endocrine Glands on the Skin."

Tuesday, August 28, 8 p.m.: "The Status of Therapeutic Dietetics in Medicine."

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Course in Occupational Medicine.

THE Post-Graduate Committee in Medicine in the University of Sydney wishes to announce that a course in occupational medicine will be held by the School of Public Health and Tropical Medicine at the University of Sydney from September 26, 1951, to November 21, 1951, for nine half-day periods. Five of the periods will be lecture-demonstrations to be held at the School of Public Health and Tropical Medicine. The four other afternoons will be devoted to field visits to industries.

Dr. G. C. Smith, Lecturer in Industrial Health, of the School of Public Health, will be the supervisor of the course.

The fee for enrolment will be £1 1s., and those wishing to attend should enrol with the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 5238, BW 7483.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 44, of June 28, 1944.

NAVAL FORCES OF THE COMMONWEALTH.

Permanent Naval Forces of the Commonwealth (Sea-Going Forces).

Appointment.—Edward Henry Roffey is appointed Surgeon Lieutenant (for short service), dated 4th June, 1951.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Volunteer Reserve.

Promotion.—Surgeon Lieutenant Ian Campbell Galbraith is promoted to the rank of Surgeon Lieutenant-Commander, dated 25th February, 1951.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force: Medical Branch.

The appointment of Squadron Leader (Temporary Wing Commander) D. McK. McNab (033132) is terminated on medical grounds, 2nd April, 1951.

Active Citizen Air Force: Medical Branch.

Flight Lieutenant W. A. Newnham (05978) is transferred to the Reserve, 10th February, 1951.

The following are appointed to commissions, 27th January, 1951, with the rank of Flight Lieutenant: John Wilford Walsh (051337), Terence Desmond Bourke (051338).

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 30, 1951.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.[2]	Australia.[2]
Ankylostomiasis	*	..	..	..	..	..	..	..	..
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	..	..	1(1)	..	..	1(1)	..	..	2
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	5(5)	..	..	..	..	..	5
Diphtheria	6(4)	7(7)	7(6)	..	5(4)	..	..	..	25
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	..	7(6)	..	2(2)	..	..	..	9
Encephalitis Lethargica	..	1	..	..	..	..	..	..	1
Erysipelas	*	*	*	1	*	*	..	..	1
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	..	*	*	*	*	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	..	..	..	..	..	..	..	..
Measles	*	*	*	74(24)	*	*	..	..	74
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	24(5)	10(3)	17(8)	36(25)	2(2)	2(1)	..	..	91
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	..	3(3)	..	..	..	..	3
Rubella(*c*)	*	*	*	*	1(1)	*	..	..	1
Scarlet Fever	8(1)	15(10)	5(4)	3(3)	5(2)	11(7)	..	..	47
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	..	*	1	*	*	*	1
Trachoma	*	..	..	*	*	*	*	*	..
Tuberculosis(*d*)	25(24)	12(8)	11(6)	10(9)	11(8)	4(3)	..	..	73
Typhoid Fever(*e*)	..	..	..	..	..	..	..	..	..
Typhus (Endemic)(*f*)	..	..	2	..	..	..	..	..	2
Undulant Fever	..	..	..	..	..	..	..	..	..
Weil's Disease(*g*)	*	*	2(1)	*	*	*	*	*	2
Whooping Cough	*	*	*	3(2)	*	*	..	..	3
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.

[2] Figures not available.

[3] Figures incomplete owing to absence of returns from the Northern Territory and Australian Capital Territory.

* Not notifiable.

(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Medical Prizes.

THE STAWELL PRIZE.

THE Stawell Prize, a memorial to Sir Richard Stawell, is open for competition. The amount of the prize is £30 (thirty pounds). The conditions are as follows:

1. The prize shall be awarded to the writer of the essay adjudged to be the best on a subject selected annually.
2. The subject for 1951 is "The Problems of Hepatitis".
3. The dissertation should be based on personal observation and experience of the writer.
4. The competition is open to graduates of any Australian university.
5. The trustees reserve the right to withhold the award.
6. Essays must be delivered to the Medical Secretary, British Medical Association (Victorian Branch), by 4 p.m. on March 31, 1952.
7. Each essay must be typewritten or printed and must not exceed 75,000 words in length.
8. Each essay must be distinguished by a motto and must be accompanied by a sealed envelope marked by the same motto, containing the name and address of the author.
9. The trustees reserve the right to publish the prize essay.

Obituary.

HENRY BYAM ELLERTON.

WE regret to announce the death of Dr. Henry Byam Ellerton, which occurred on July 16, 1951, at Balgowlah, New South Wales.

HERBERT HENRY ERNEST RUSSELL.

WE regret to announce the death of Dr. Herbert Henry Ernest Russell, which occurred on July 10, 1951, at Unley, South Australia.

WILLIAM WATKIN WINN CHAPLIN.

WE regret to announce the death of Dr. William Watkin Winn Chaplin, which occurred on July 9, 1951, at Melbourne.

Notice.

OWING to the zoning of electric power the meeting of the Section of Pædiatrics of the New South Wales Branch of the British Medical Association, which was to have been held on Thursday, August 2, 1951, has been postponed until August 9.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Bedingfeld, Richard Collier, M.B., B.S., 1951 (Univ. Sydney), Wellington District Hospital, Wellington.

The undermentioned have been elected members of the New South Wales Branch of the British Medical Association:

Benecke, John, M.B., B.S., 1950 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.
Collins, John James, M.B., B.S., 1951 (Univ. Sydney), Lewisham Hospital, Lewisham.
Conley, Valda Mary, M.B., B.S., 1951 (Univ. Sydney), Tweed District Hospital, Murwillumbah.
Cook, James Cecil Murray, M.B., B.S., 1950 (Univ. Sydney), 23 Killarney Street, Mosman.
Crane, Henry Graham Elliott, M.B., B.S., 1951 (Univ. Sydney), 20 Nicholson Street, Burwood.
Friendship, Colin James, M.B., B.S., 1951 (Univ. Sydney), Canterbury District Memorial Hospital, Campsie.
Gale, Barry Mitchell, M.B., B.S., 1951 (Univ. Sydney), Auburn District Hospital, Auburn.
Gunner, Bruce Warren, M.B., B.S., 1951 (Univ. Sydney), Royal Newcastle Hospital, Newcastle.
Hickie, John Bernard, M.B., B.S., 1948 (Univ. Sydney), 34 Gurner Street, Paddington.
Jonas, Siegbert, M.B., B.S., 1951 (Univ. Sydney), 178 Elizabeth Street, Sydney.
Meldrum, William Arthur, M.B., B.S., 1951 (Univ. Sydney), Lithgow District Hospital, Lithgow.
Mitchell, Robert Wentworth, M.B., B.S., 1951 (Univ. Sydney), Base Hospital, Dubbo.

Diary for the Month.

AUG. 1.—Western Australian Branch, B.M.A.: Council Meeting.
AUG. 2.—South Australian Branch, B.M.A.: Council Meeting.
AUG. 3.—Queensland Branch, B.M.A.: Branch Meeting.
AUG. 3.—Tasmanian Branch, B.M.A.: Council Meeting.
AUG. 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.
AUG. 10.—Queensland Branch, B.M.A.: Council Meeting.
AUG. 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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